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SCIENCE AND TECHNOLOGY

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6 MAY 1987

JAPAN REPORT

SCIENCE AND TECHNOLOGY

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APPLICATIONS OF ENZYME IMMOBILIZING POLYMERIC MEMBRANES DISCUSSED

Tokyo BIO INDUSTRY in Japanese Aug, Sep 86

[Two-part article by Tadashi Uragami, assistant professor, Faculty of Engineering, Kansai University]

[Aug 86 pp 22-32]

[Text] Manufacturing and Evaluation Methods

Recently, interest in biotechnology, bioengineering, and bioindustry has heightened worldwide; they are expected to have wide applications in various fields. Hence, the utilization of enzyme immobilizing polymeric membranes with separation functions, a technique in the boundary between enzyme engineering and membrane engineering, may be considered a new field of science. This article considers why separation functions based on immobilized enzymes are needed and briefly describes the preparation of enzyme immobilized membranes based on the conventional manufacturing method of immobilized enzymes, their properties, and their performance evaluation.

1. Why Enzyme Immobilizing Polymeric Membranes With Separation Functions Are Needed

1.1 Immobilization of Enzymes

Consisting of proteins, an enzyme functions as a catalyst in living organisms, and facilitates various chemical reactions. Enzymes catalyze various reactions, and they show excellent catalytic activity under mild conditions of normal temperature and pressure, facilitating catalysis at high efficiency. Their features are high functional singularities such as matrix specificity, orientation specificity, three-dimensional specificity, and reaction specificity, and they differ from catalysts used in ordinary chemical reactions.

Enzymatic functions are already being used in a broad spectrum of fields, such as the food industry, textile industry, leather industry, medical industry, and medical treatment industry. Their applications such as assembling catalysts from the reaction processes demanded by modern society, for example in energy-saving, resource-saving, and environmental preservation, are also awaited with great expectation. With recent rapid advances in biochemistry and genetic engineering, progress has been seen in the elucidation of

enzymatic function mechanisms, discovery of new enzymes, new enzyme manufacturing and refinement methods. Furthermore, studies are being made on new utilization methods.

The biggest drawback of enzymes is that they can only be used under a mild condition and that they are unstable in strong acids, strong bases, organic solvents, and heat. Ordinarily, an enzyme docks with a substrate in an aqueous solution, but recovering the enzyme from the solution after reactions entails difficulty, and utilization of expensive enzymes as disposable products is uneconomical.

Therefore, from the consideration that if enzymes are kept in a stable state not soluble in water while maintaining their activity as high as possible, they can be utilized repeatedly; enzyme immobilization methods have been proposed.[1-3]

1.2 Enzyme Immobilizing Membranes

The objective of enzyme immobilizing membranes is basically the same as that of immobilized enzymes, but they aim for enhanced function. As shown in Figure 1, when the enzyme E is immobilized onto a polymeric membrane and the substrate S is added, the substrate is dissolved by the enzyme's substrate specificity and at the same time is separated into substrate and product P via the membrane. The need for an enzyme immobilizing membrane heightens especially when, as shown in Figure 1, the two functions of reaction and separation are demanded simultaneously.

As shown in Figure 2, for example, where although the polymeric substrate does not filter through the membrane, it is dissolved by the enzyme immobilized on the membrane surface and the low-molecular products produced in the process penetrate through the membrane.

An enzyme immobilizing membrane is a system where breakdown of the substrate and separation of the low molecular products occur continuously. Also in cases, as shown in Figure 3, where the objective is to obtain from a mixture of high molecular compounds and low molecular compounds, with the high molecular compounds being separated by the membrane, the products produced by the catalytic action of the enzyme on the low molecular compounds when passing through the membrane, the need for an enzyme immobilizing separation membrane increases further.

Theoretically, on the other hand, enzyme immobilizing separation membranes are also objects of interest as models of the membrane enzymes that are taking part in selective and active transportation in living cells.

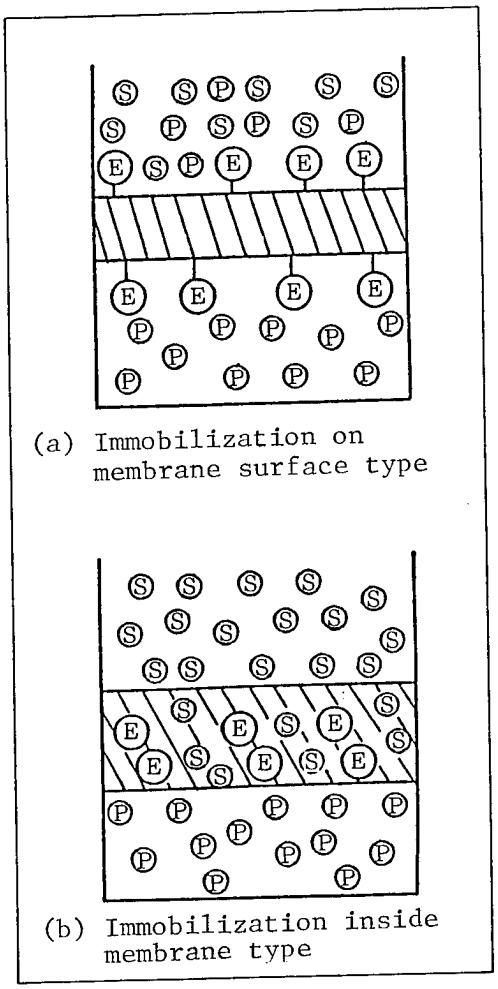


Figure 1. Enzyme Immobilizing Polymeric Membranes With Separation Functions
E: enzyme; S: substrate; P: product

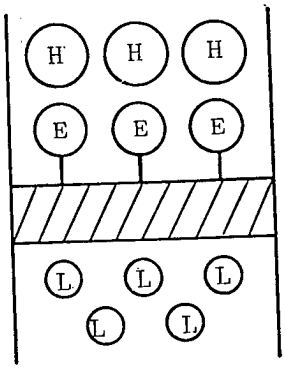


Figure 2. Enzyme Immobilizing Polymeric Membrane With Separation Functions for Breakdown of High Molecular Substrate
H: high; L: low

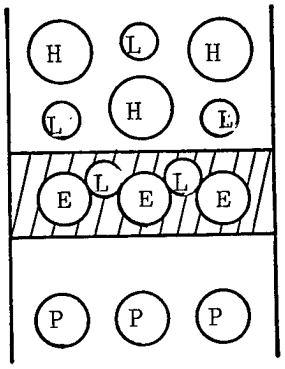


Figure 3. Enzyme Immobilizing Polymeric Membrane With Separation Functions for Breakdown of Low Molecular Substrate
H: high; L: low; P: product

2. Preparation of Enzyme Immobilized Membranes

Preparation of enzyme immobilized membranes is conducted basically according to the preparation method of immobilized enzymes. For an enzyme in an immobilized state to fully display its catalytic action, the molecule has to be immobilized in a way in which the amino acid residues making up the active center of the enzyme proteins and their high-dimensional structures are not altered.

Many enzyme immobilization methods have been proposed, and they are broadly classified into the following three categories of: 1) binding onto a support method; 2) bridging method; and 3) inclusion method.[1-3]

Enzyme immobilized membranes are prepared according to the enzyme immobilization methods mentioned above, and they come in specimens as shown in Figure 4.[4]

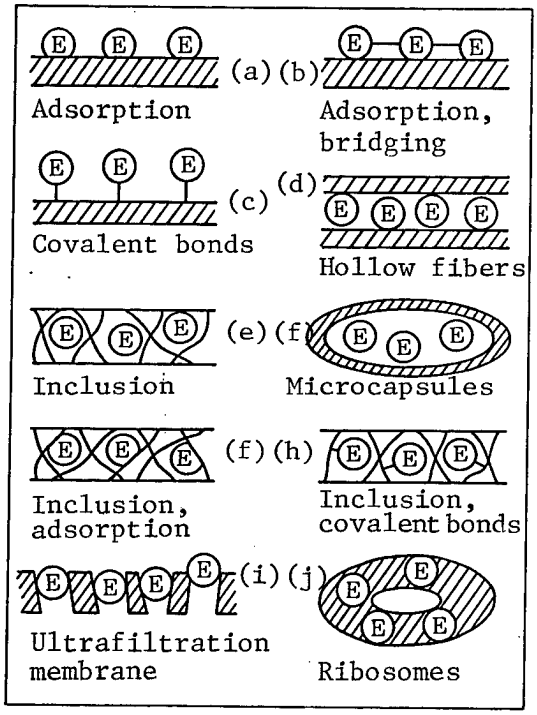


Figure 4. Kinds of Enzyme Immobilized Membranes

In Figure 4 (a) is a method in which an enzyme is adsorbed and immobilized onto a high molecular support membrane and (b) is a method in which the immobilized enzyme in (a) is further bridged; (c) is a method in which the enzyme is attached to the support membrane by means of covalent bonds; (d) is a sort of inclusion method in which the enzyme is trapped inside a membrane of hollow fibers; (3) is a method in which the enzyme is taken into and immobilized onto a polymer matrix; (f) is a microcapsule type inclusion membrane where the enzyme is coated with a polymeric membrane; (g) is a method in which the

enzyme inclusion-immobilized onto the polymeric membrane mentioned in (e) is further adsorbed and immobilized by means of ionic bonds; (h) is a complex immobilization membrane in which the enzyme immobilized by the method in (e) is further immobilized by means of covalent bonds; (i) is a sort of adsorption immobilized membrane in which the enzyme is immobilized into cavities of an ultrafiltration membrane; and (j) is an inclusion type membrane in which the enzyme is immobilized inside ribosomes. These manufacturing methods of enzyme immobilized membranes each have characteristic features.

2.1 Binding Onto a Support Method

Included in this technique are the three bonding methods: 1) physical adsorption; 2) ionic bonds; and 3) covalent bonds. This technique, under which an enzyme is immobilized by bonding onto a support insoluble in water, has been tried over a long period of time with many enzymes.

(1) Selection of support

When immobilizing an enzyme by means of this technique, it is only natural to select a bonding and immobilizing conditon that protects the enzyme from losing its activity but full attention also needs to be paid to the selection of support used. In other words, in preparing an enzyme immobilized membrane, the amount of enzyme to be immobilized, as well as the activity of the enzyme, is affected by the polymeric membrane being used for support.

The type of polymeric membrane support selected is determined by the property of the enzyme to be immobilized. But, when the prepared enzyme immobilized membrane is required to have a separation capability, ample consideration needs to be given to the physical and chemical structures of the polymeric membrane support, with respect to details as shown in Table 1. As for the physical structure of a polymeric membrane, the amount of enzyme immobilized is greatly determined by the membrane's whole diameter, its surface area and its thickness, with a large effect on its separation function.

Table 1. Properties of Polymeric Membrane Support

Physical structure
Hole diameter, surface area, membrane thickness, etc.
Chemical structure
Balance between hydrophilic property and hydrophobic property
Chemical composition, etc.

As for the chemical structure of a polymeric membrane the amount of enzyme immobilized is affected by the chemical composition of the membrane surface and its interior as well as the balance between hydrophilic and hydrophobic properties, which in turn are reflected in the enzyme immobilized membrane's

permeability and separation characteristics. Among membrane materials for polymer membrane supports are both natural polymers and synthetic polymers, and which polymer is used is determined by the concerned enzyme immobilization method.

(2) Comparing the methods of bonding enzymes to supports

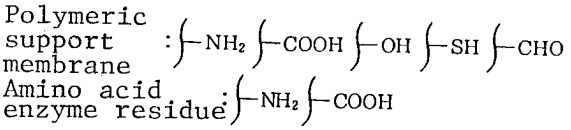
Table 2 lists the advantages and disadvantages of immobilizing enzymes by binding them onto a support.

Table 2. Advantages and Disadvantages of Support Bonding Methods

Immobilizing method	Active center, change in high-dimensional structure	Level of immobilization
Physical adsorption	A	C
Ionic bonds	A	B
Covalent bonds	B	A

In the physical adsorption method in which an enzyme is physically adsorbed for immobilization onto a polymeric membrane support by means of the mutual action between hydrophobic bonds, or in the ionic bonding method in which an enzyme is ionically bonded for immobilization to a water-insoluble polymeric membrane support with ion exchange groups, the immobilizing condition of the enzyme is mild, so there is little change in the active center of the enzyme or in its high-dimensional structure. The drawback is that since the mutual action between enzyme sometimes dissociates itself from the support membrane. This depends on the pH of the solution or the kind of buffer solution, or when the ionic strength is high, and the level of immobilization, therefore, is not very strong. But, there is a case where the ionic bonding method is employed for industrial production of L-amino acid,[5] in which a polysaccharide (DEAE-Sephadex) of negative ion exchange has amino "acylase" immobilized in it. So, with the proper combination of enzyme and polymeric membrane support, immobilization may be possible.

The covalent bonding method is an immobilizing method in which an enzyme is attached to a polymeric membrane support by covalent bonds. When immobilizing an enzyme onto a polymeric membrane using this technique, the following functional groups need to be introduced onto the membrane surface and its interior.



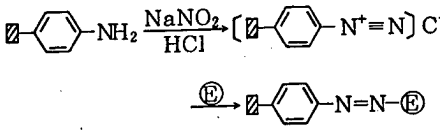
This is for helping facilitate the reaction between the functional groups, the amino group and the carboxyl group generally arising from the amino acid residue to facilitate immobilization.

Compared with the aforementioned physical adsorption and ionic bonding methods, the covalent bonding method is complex with respect to setting the reaction condition and manipulation of the reaction. Furthermore, since with this method the processing condition for immobilizing the enzyme is relatively demanding, the possibilities are great where the high-dimensional structures of the enzyme proteins and the active center undergo changes. But provided the processing condition of enzyme immobilization is set at as mild a condition as possible and the defects mentioned above are minimized as much as possible, the method has advantages: since in the enzyme immobilizing membrane obtained this way, the enzyme is firmly bound to the support polymeric membrane by covalent bonds, it does not dissociate itself regardless of the pH of the solution or the type of buffer solution; and even if it comes into contact with a high-density substrate solution or salt solution, the enzyme scarcely dissociates itself.

(3) Bonding methods of covalent bonds

Among the principal methods for immobilization of enzymes by means of covalent bonds are the diazo, peptide, and alkylation methods.[1-3]

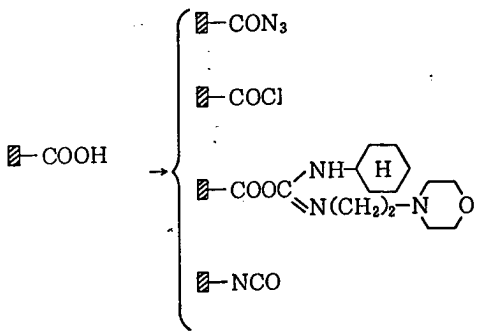
With the diazo method, as shown in formula (1), a polymeric membrane support with an aromatic amino group is turned into a diazonium compound and the enzyme is immobilized by means of diazo coupling.



(1)

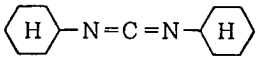
The peptide method is a technique where immobilization is achieved by forming peptide bonds between the polymeric membrane support and enzyme proteins, and it comes in two varieties.

With the first variety, as shown in formula (2), a polymeric support membrane containing carboxyl is turned into acid azide, acid chloride, carbodiimide, and isocyanate derivatives, and they form peptide bonds with free amino groups contained in the enzyme proteins.

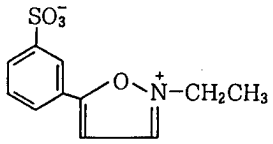


(2)

With the second variety, using dicyclohexyl-carbodiimide used in peptide synthesis [1] or Woodward's reagent K (N-ethyl-5-phenylisoxazolium-3'-sulfonate) [2], peptide bonds are formed between a polymeric membrane support containing amino groups or carboxyl groups and free carboxyl groups or amino groups of the enzyme proteins.

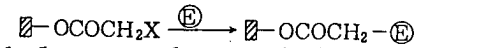


(1)

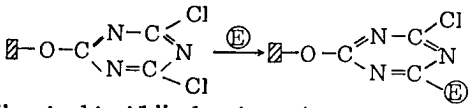


(2)

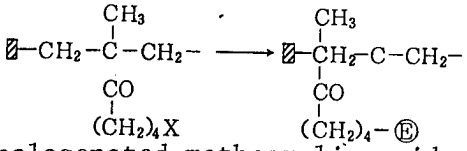
Polymeric membrane supports used in the alkylation method of bonding are those provided with functional groups of high reactivity, such as halogenated acetyl derivatives, "triadinil" derivatives, and halogenated methacrylic acid derivatives, and enzymes are immobilized by alkylation of those functional groups with free amino groups contained in the enzyme proteins and phenolic hydroxyl groups, as shown in formulas (3) through (5).



halogenated acetyl derivatives (3)



"triadinil" derivatives (4)

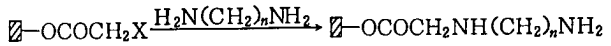


halogenated methacrylic acid derivatives (5)

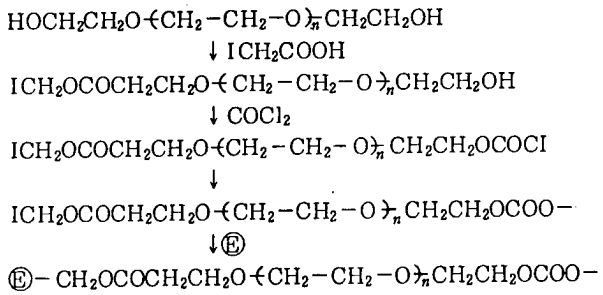
(4) Insertion of spacers

When immobilizing an enzyme onto a polymeric membrane support, it sometimes occurs that the enzyme's activity is manifested more easily if the enzyme's molecules are immobilized away from the membrane support. In such a case, inserting a spacer between the enzyme molecules and the polymeric membrane support helps.

For example, as shown in formula (3), halogenated acetyl derivatives react with diamine for amination as shown in formula (6), and the amino group's reactivity is taken advantage of in order to immobilize the enzyme. Controls of the manifestation of the enzymatic activity are possible by adjusting the length of methylene bonds.



(6)



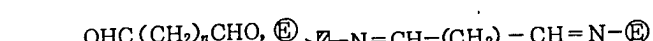
(7)

From such a point of view, a new method has been reported[6] in which, as shown in formula (7), the hydroxyl group, one of the terminals of ethylene glycol, is turned into iodoacetic acid ester while the other terminal is turned into "chloroformart" to be combined with cellulose, which results in the synthesis of iodoacetic acid ester cellulose of polyethylene glycol, and the derivative is used as the support on which to combine an enzyme. The method is an interesting enzyme immobilizing technique in cases where enzymatic function needs to be expressed while maintaining the polymeric membrane support's permeability and separation functions intact.

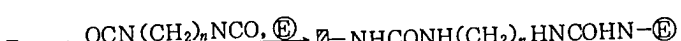
(5) Method of binding to support using bridging reagents

One method of binding enzymes onto a support is in which the enzyme is immobilized onto a polymeric membrane support using a bridging reagent. Under this method, a reagent provided with two or more functional groups that work on the free amino group is used, and enzyme immobilization is achieved by crosslinking the polymeric support membrane provided by the amino group with the amino groups inside the enzyme proteins.

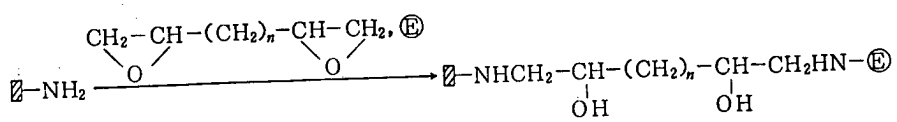
With this method, dialdehydes like glutaraldehyde are used as bridging reagents. As shown in formula (8), enzyme immobilization is most commonly achieved by forming Schiff bases between the amino groups of the polymeric membrane support and amino groups of the enzyme proteins. But recently, as shown in formulas (9) and (10), enzyme immobilization using such bridging reagents and diisocyanate and "diglyceride" compounds are drawing attention.



(8)



(9)



(10)

When trying to immobilize an enzyme onto a polymeric support using dialdehyde, diisocyanate, or diglyceride compounds as the bridging reagent, there occur, depending on the conditions, not only bridging reactions between the polymeric support and enzyme molecules, but also bridging between polymeric supports themselves. In such a case, when the polymeric support is a membrane, permeability and separation characteristics of the polymeric membrane itself are sometimes affected. Therefore, when manufacturing an enzyme immobilized polymeric membrane with separation functions, attention needs to be paid not only to the immobilization of the enzyme but also to the controls of the membrane's permeability and separation characteristics.

2.2 Bridging Method

As with the covalent bonding method of the aforementioned binding-to-support methods, the bridging method is a technique where an enzyme is immobilized by chemical bonds. In this case, however, no polymeric support is employed, and an enzyme is immobilized by means of bridging reactions alone, and it is furthermore not soluble in water. Therefore, with this method, enzyme molecules are crosslinked with each other using a reagent provided with two or more functional groups of reactivity to form an enzyme immobilized membrane.

If the membrane is to have the functions of permeability and separation, further studies are needed on the method and conditions of membrane-making, but it is a promising membrane for use as a thin-film enzyme immobilized membrane with separation functions.

2.3 Inclusion Method

This method comes in two types: One is the lattice type in which immobilization is realized by entrapping, as shown in Figure 4(e), an enzyme into a fine lattice matrix of polymer gels, keeping it in a state unable to dissociate itself. The other is the microcapsule type in which, as shown in Figure 4(f), an enzyme is coated with a semitransparent polymeric membrane.

Differing from the aforementioned binding-to-support method and the bridging method, under this process no bonding reaction occurs between the polymeric support and the enzyme proteins. Consequently, from the viewpoint of maintaining the enzyme's activity it has many advantages. The technique is also handy since it allows easy immobilization of various kinds of enzymes. But in cases where a membrane is grown by a polymerization reaction while an enzyme is being inclusion-immobilized at the same time, care needs to be taken lest the enzyme's activity decreases.

When a polymerization reaction takes advantage of radiation such as X-rays and gamma rays, the process can be conducted under even a frozen state, keeping to a minimum the enzyme's loss of activity,[7-9] and enzyme immobilization onto a membrane type support can easily be obtained.

(1) Examples of various inclusion methods

A prepolymer of optically crosslinking polyethylene glycol with "acryloile" groups on both ends is added with a photosensitization agent and a water solution of enzyme; the mixture is cast onto a polymeric film and irradiated with near ultraviolet rays for a few minutes; then it turns into a gel, thus forming an enzyme immobilized membrane.[10]

Another method is to take advantage of the phenomenon that a copolymer of polyethylene glycol with toluenediisocyanate on both ends and polypropylene glycol easily crosslinks forming urea bonds under water, and the copolymer is added with an enzyme water solution to prepare film for an enzyme immobilized gel state.[11]

An enzyme is added to a hydration suspended solution of collagen and electrodes are inserted into the liquid. When a direct current is applied, an enzyme immobilized collagen membrane is formed at the cathode.[12] When the aforementioned collagen suspended solution containing an enzyme is spread over a flat panel and dried, the end product is an enzyme immobilized collagen membrane. In case the enzyme elutes and dissociates itself from the membrane, bridging is applied to the membrane surface using glutaraldehyde, which prevents the enzyme from dissociating.[4,13]

(2) Lamination type enzyme immobilized membrane based on polyion complex

When polycation, a high molecular electrolyte, is mixed with a water solution of polyanion, a polyion complex insoluble in water is produced. When there exists an enzyme water solution while the polyion complex is being formed, the enzyme molecules are immobilized onto the matrix of the polyion complex. However, mixing polycation with polyanion immediately leads to the formation of a polyion complex, and thus it is very difficult to obtain membranous material.

The author then turned efforts toward solution of the problem of immobilizing enzymes without using reagents or without subjecting them to any treatment, which are the causes of lowered enzymatic activity. As one attempt at putting to good use features of enzyme immobilized membranes, we started study on utilizing an ultrafine infiltration method, one of the membrane separation techniques, and set about forming an ultrafine filtration type enzyme immobilized membrane by immobilizing an enzyme onto the matrix of a polyion complex.[14,15]

In other words, fourth-grade chitosan (polycation) and polyacrylic acid sodium (polyanion) are separately prepared into solutions of required concentrations using a water solution of sodium bromide, and the two solutions are mixed until their ion exchange capacities are equal. Since the existence of sodium bromide constrains the formation of a polyion complex, the mixed solution remains uniform. When the mixed solution is poured onto a microporous film set inside an ultrafiltration cell for ultrafiltration, the sodium bromide used as the retarder for the formation of a polyion complex is removed along with water.

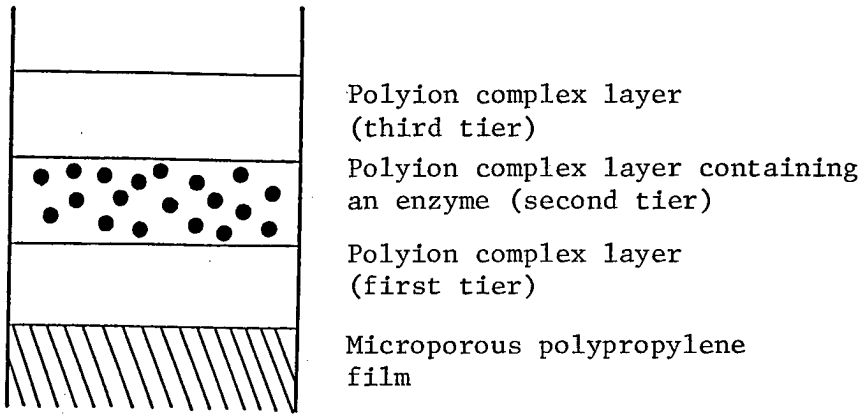


Figure 5. Lamination Type Enzyme Immobilized Membrane

As shown in Figure 5, a polyion complex of uniform quality is formed on the first layer. Next, the aforementioned mixed solution containing an enzyme is subjected to ultrafiltration, and a layer of polyion complex is formed on the second tier. On the third tier a layer of polyion complex similar to that in the first tier accumulates. The third layer prevents products produced by enzymatic reactions inside the enzyme immobilized membrane from shifting to the side of the supply solution, and is effective when the desired products will not mix with the substrate solution.

(3) Microencapsulation

Immobilization of enzymes in microcapsules is considered to be the first attempt at enzyme immobilized membranes with separation functions. Main techniques employed in the microencapsulation method where immobilization is achieved by enclosing enzymes in a semipermeable membrane are the interfacial polymerization, inside-a-liquid dehydration and phase separation, and each has advantages and disadvantages. Details are omitted here, and the reader is advised to refer to references[1,3,16] for details.

3. Properties of Enzyme Immobilized Membranes and Their Performance Evaluations

The understanding of how an enzyme alters its properties when it is immobilized onto a support is very important in considering applications of enzyme immobilized membranes. The causes giving rise to an immobilized enzyme changing its properties are, as shown in Table 3, mainly two. The first is the alteration of the enzyme itself,and the second is the physical and chemical properties of the immobilization support membrane.

Therefore, when an enzymatic reaction occurs using an enzyme immobilized membrane, it is meaningful to understand how the enzyme alters its properties depending on the reaction condition--condition dependency, as well as the rate constant from the point of view of kinetics.

Table 3. Changes in Enzymatic Properties of Enzyme Immobilized Membrane

1) Alterations of the enzyme itself	Modification of the amino acid residue in the active center; changes in high-dimensional structures; changes in the state of electric charge
2) Physical and chemical properties of immobilization support	Formation of a diffused layer in the periphery of enzyme immobilization; steric hindrance to the support; electrostatic mutual reactions

3.1 Stability

One of the objectives of an enzyme immobilization is to increase the stability of the enzyme. Whether or not an enzyme immobilized membrane can be used continuously on a stable basis is an important evaluation factor in using it in practical applications.

Generally speaking, the higher the frequency with which an enzyme is used, the shorter the life of the enzyme immobilized membrane.[1,17] But, provided the properties of the enzyme itself and its immobilization method are matched well, on some occasion the membrane can be used continuously for a long period of time.[18] By the immobilization method, the stability of an enzyme increases in the following order, of covalent bonds, inclusion, and adsorption.[17,19]

Immobilization of an enzyme in many cases increases its stability against various reagents. One of the contributing factors is that immobilization increases the rigidity of the enzyme protein structures, making them less vulnerable to the inhibition effect of protein denaturants such as urea.[20,22] It also owes to the fact that because of the effect of steric hindrance brought about by immobilization of an enzyme, high molecular inhibitors to enzymes have difficulty getting closer to the enzyme.[20,23]

As with catalysts used in ordinary chemical reactions, enzymes increase their reaction speed in keeping with increases in the reaction temperature. However, enzymes generally are not stable if heated. Therefore, if immobilization of an enzyme gives it a high resistance to heat, it would greatly facilitate the protein's industrial use. Most enzymes increase their stability to heat when immobilized,[21,24] but correlations between immobilization and heat stability have not been observed.

When an enzyme is immobilized, its resistance to various proteolytic enzymes increases.[21,25,26] This is because the immobilization protects specific amino acid residues in the enzyme proteins and inhibits the catalytic action of enzymes that work specifically on the amino acid residues thanks to steric hindrance. In other words, autolysis is less likely to occur.[27-29]

3.2 Substrate Specificity

When enzymes are immobilized, their activity in most cases goes down and occasionally their specificity to substrates undergoes alterations. Especially when an enzyme that works on high molecular substrates like proteolytic enzymes and amylases is immobilized by means of the binding-to-support method, its specificity to substrates changes greatly, generally lowering its activity.[20,28,30] This is because immobilization of an enzyme onto a polymeric membrane support gives rise to steric hindrance, making it harder for the high molecular substrate to get close to the enzyme molecules.

3.3 Dependency on pH

Catalytic functions of enzymes are affected greatly by the external environments, such as pH, temperature and ionic solution strength, and pH in particular has a great impact. Therefore, it is necessary to study what change immobilization of an enzyme will bring about in the pH dependency of the enzymatic reaction. Shifts in the optimal pH for enzymatic reactions in the wake of enzyme immobilization are sometimes caused by electrostatic properties of the polymeric support.[21,31-35]

3.4 Performance Evaluations by Electrodes[17,19,36]

The electrode method is mainly used for performance evaluations of enzyme immobilized membranes for use in biosensors, but it can be applied to the stability evaluation of ordinary enzyme immobilized membranes. The stability of glucose oxidase immobilized membranes manufactured by adsorption, inclusion, and covalent bond methods for use as enzyme immobilized membranes in biosensors was examined by the electrode method.[17]

That is, enzyme electrodes attached with glucose oxidase immobilized membranes were placed into a buffer solution containing a required density of glucose, and outputs from the electrodes were recorded at required times to study and compare the activities of those immobilized membranes. The stability strength was due to the covalent bonds, inclusion and adsorption. In the case of enzyme immobilized membranes prepared by means of the adsorption method, no dissociation of the enzyme even when the membrane surface was coated with a dialysis membrane was observed.

3.5 Dynamical Performance Evaluation[1,3,4,14,15,17,37,38]

The differences in properties between enzyme immobilized membranes and free enzymes arise not only from the effects of structural changes of the enzyme molecules accompanying immobilization and steric hindrance but also are affected by electrostatic mutual reactions and transmission resistance between the substrate and products on the one hand and the immobilized polymeric support membrane on the other. Therefore, measuring the dynamical constant of an enzyme immobilized membrane as a measurement of reaction speed is an important evaluation method for forecasting the state of reaction by the enzyme immobilized membrane.

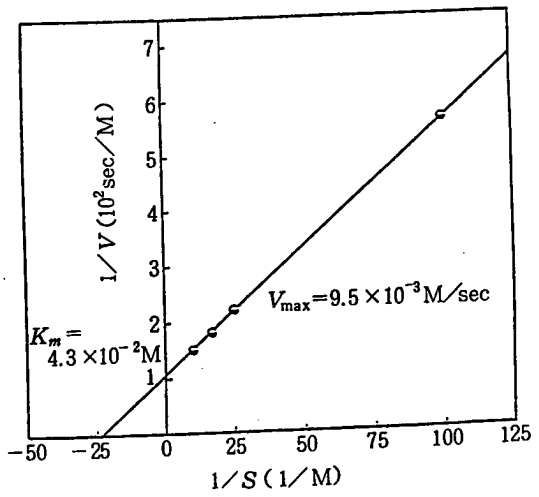


Figure 6. Lineweaver-Burk Plot Showing Hydrolysis Reactions of Urea by Urease Immobilized Polyion Complex Membrane

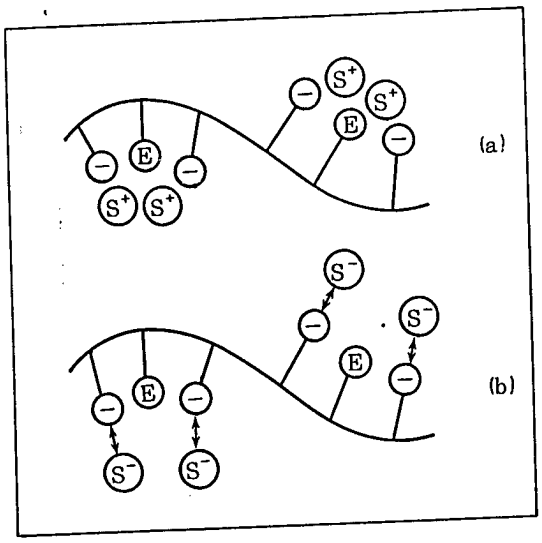


Figure 7. Effect of Charges Applied to High Molecules of the Support on Enzymatic Reaction

Figure 6 shows a Lineweaver-Burk plot showing hydrolysis of urea through a membrane which has urease immobilized inside a polyion complex by means of the ultrafiltration method.[14] The apparent Michaelis constant of the urease immobilized membrane is not so different from that of the urea hydrolysis reaction of free urease, but the immobilized membrane reaction speed was about 700 times faster.

Figure 7 shows a schematic diagram in which an enzyme is immobilized onto a polyanionic support. In the case of (a) in the figure, the substrate is charged positively, increasing the electrostatic mutual reaction, so the substrate concentrations in the neighborhood of the immobilized enzyme are higher than those in the external solution. Therefore, enzymatic reactions occur under higher concentrations than the substrate concentrations actually being used, and the apparent Michaelis constant shows a small value.[30]

In the case of (b), the substrate is charged negatively, leading to a repulsion between it and the polyanionic suport, so contrary to (a), the apparent Michaelis constant becomes large.[39]

Table 4 shows the relationship between the particle diameter and the Michaelis constant in the hydrolysis of maltose by immobilized glucoamylase.[40] The smaller the particle diameter, the smaller the Michaelis constant. This is assumed to come from the belief that as the particle diameter becomes smaller, the effect the internal diffusion of the substrate has on the reaction speed diminishes, getting closer to the original enzyme's Michaelis constant.

Table 4. Effect of Particle Diameter of Immobilized Glucoamylase

	Michaelis constant, K_m (mM)		
	Particle diameter of immobilized enzyme		
Original enzyme	15 μm	15-55 μm	70-190 μm
0.9	1.35	1.6	2.15

3.6 Performance Evaluation of Membrane's Permeability[17,41]

Permeability of the enzyme immobilized membrane, that is, the capacity of the substrate and generated products which pass through the membrane, are very important in evaluating its performance. Many factors influence the membrane's permeability, primarily the membrane thickness, substrate density, permeation temperature, pressure, and pH.

As shown in Figure 8, a urease immobilized collagen membrane was placed in the boundary between the L and R sides of a diaphragm type cell for a diffusion experiment; a water solution of urea was poured into the L side as a substrate, and the state of ammonium diffusion which was produced as a result of the breakdown of urea by the work of the immobilized urease into right and left sides was measured. Seventy-five percent of all the ammonium thus produced diffused to the L side and 25 percent diffused to the R side. This indicates that almost all enzymatic reactions took place in the L side of the enzyme immobilized membrane. In other words, the result suggests that compared with the substrate's diffusion, the enzymatic reaction takes place at an extremely fast speed.

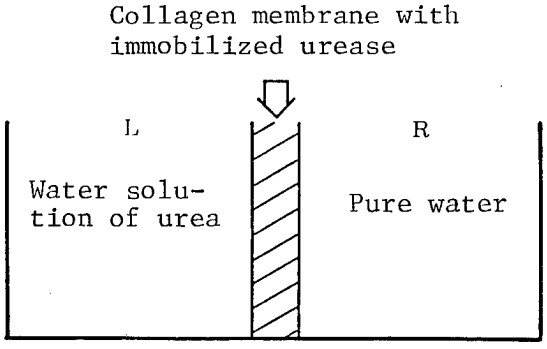


Figure 8. Performance Evaluation Based on Membranes Permeability

The foregoing described the need for enzyme immobilized membranes, their preparation methods and their performance evaluation methods from various angles, and all this teaches us again the importance of selecting the proper preparation method of enzyme immobilized membranes with rational functions when one is going to use an enzyme immobilized membrane for some purpose.

In the next issue, applications of enzyme immobilized membranes with separation functions, their prospects, and problems will be described.

FOOTNOTES

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[Sep 86 pp 32-44]

[Text] Applications and Prospects

The greatest features of enzyme immobilized membranes with separation functions can be seen in the dual utilization of the enzyme's specificity to a specific substrate and the polymeric membrane's separation functions. Given their features, as such, enzyme immobilized membranes with separation functions are expected to find wide application in various fields. Described in this [portion of the] paper are possible applications in such fields as hydrolysis reaction, analysis, medicine, environmental purification, and transportation through condensation, as well as their prospects and problems.

4. Possible Applications of Enzyme Immobilized Membranes With Separation Functions in Various Fields

As described in the [previous part of this] article,[42] an enzyme immobilized membrane is a sort of immobilized enzyme in which an enzyme is fixed onto a membranous support by some means. It possesses not only the catalytic function associated with the immobilized enzyme but also permeability and separation functions coming from the membranous support. That is, an enzyme immobilized membrane facilitates material separation thanks to the membrane's selective permeability and is also easy to transport. It is not only advantageous in terms of energy but has an added merit of not giving rise to side reactions. Furthermore, it can be operated continuously while putting to good use its large functional capacity owing to the two-dimensional spread of the membrane, and this enables it to perform such functions as permeation and separation of materials, and catalysis at high efficiency.

Given the features of enzyme immobilized membranes with separation functions as such, their potential applications are expected to be widespread in such fields as separation and purification of materials, food processing, artificial organs, clinical tests, biosensors, bioreactors and environmental purification in a broad spectrum of areas including industry, medicine, and medical treatment analysis.

4.1 Applications to Hydrolysis Reactions

The following describes the possibilities of applying enzyme immobilized membranes with separation functions in the process for obtaining glucose

from starch by hydrolysis. Conventionally, glucose has mainly been produced by the enzymatic method in which starch is hydrolyzed using glucoamylase together with either alpha or beta amylase. With this process, there, however, remain problems with respect to the enzyme separation process, substrate and products. Therefore, continuous operability was studied using immobilized enzymes and ultrafiltration membranes.[43-48]

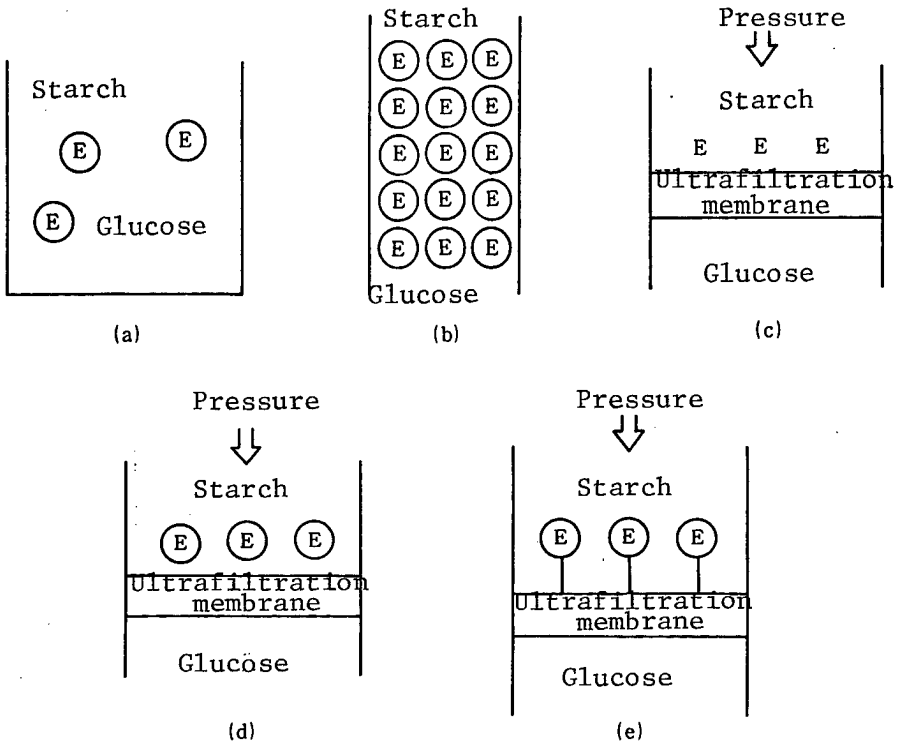

Figure 9. Hydrolysis of Starch by Various Immobilized Enzyme Systems

(1) Various immobilized enzyme systems

In Figure 9(a), immobilization of the enzyme facilitates easy separation of substrate, product, and enzyme, but separating the substrate from the product is not easy. In the case of (b) where the immobilized enzyme is contained in a column, the product can be continuously obtained by making the substrate solution move constantly. But when the viscosity of the solution is high, a pressure loss occurs and channeling inside the column, and the enzyme fails to reach its full potential. In (c) there is a process in which enzymatic reactions and an ultrafiltration membrane are used, and there the product produced as a result of hydrolysis passes through the ultrafiltration membrane, thus separating the product from the substrate. In this case, the high polymer substrate and the enzyme form a gel on the surface of the ultrafiltration membrane, lowering its permeability to a great extent and at the same time lowering the enzyme's activity. In (d) there is a process that is a combination of the process mentioned in (a) and an ultrafiltration membrane,

and is expected to have high performance provided the immobilized enzyme is amply agitated inside the substrate solution.

An ultrafiltration membrane with a physical structure that easily permits low molecular substances to pass through it but does not permit high molecular substances to filter through it, the enzyme immobilizing membrane in (e) has a chemical structure that allows easy enzyme immobilization. When using a spacer so that an enzyme functions as far away from the membrane's interface as possible and when immobilizing the enzyme onto the ultrafiltration membrane support, there occurs a hydrolysis reaction even before the high molecular substrate settles on the membrane surface. Furthermore, immobilization of the enzyme is not considered to affect the permeability and separation functions of the ultrafiltration membrane. In such a system, however, the operation pressure, temperature, pH, and agitating speed of the substrate solution are important elements. When applying an enzyme immobilized membrane in the process for fluid type ultrafiltration in particular, the flowing speed of the high molecular substrate solution is an important element, and it affects not only the probability of the immobilized enzyme making contact with the substrate but also the level of deposition of the substrate.

When obtaining glucose by the hydrolysis of cellulose, or when obtaining amino acids from proteins or polypeptides, immobilization of cellulase or a proteolytic enzyme onto an ultrafiltration membrane using a spacer is expected to enable hydrolysis and separation functions to be maintained on a continuous basis.

(2) Permeation and hydrolysis type enzyme immobilized membrane

When using an ultrafiltration membrane, the high molecular substrate tenders to polarize on the membrane surface, lowering the membrane's permeability. Therefore, in its practical application, an important consideration is that the membrane is so designed that the hydrolysis reaction progresses as the substrate is passing through the enzyme immobilized column.

By preparing a polymeric membrane with pores larger than those of the ultrafiltration membrane shown in Figure 10 from a high molecular material with a chemical structure that enables enzyme immobilization, and by further immobilizing the enzyme onto the surface of the membrane and inside the pores using a spacer since the substrate is of a high molecular substance and thus designing a permeable membrane that facilitates interactions between the substrate molecules and enzyme molecules, products can be obtained as the substrate reacts with the enzyme when passing through the membrane.

In this case, the length of time that the high molecular substrate stays inside the membrane, that is, the probability of contact between the substrate and immobilized enzyme, has the most critical impact on the enzyme immobilized membrane's performance, so that the enzyme is required to have full permeability control of the high molecular substrate. The probability of contact inside the membrane between the immobilized membrane and substrate is naturally influenced by the condition under which the substrate passes through the membrane. Selection of the operation pressure is an especially

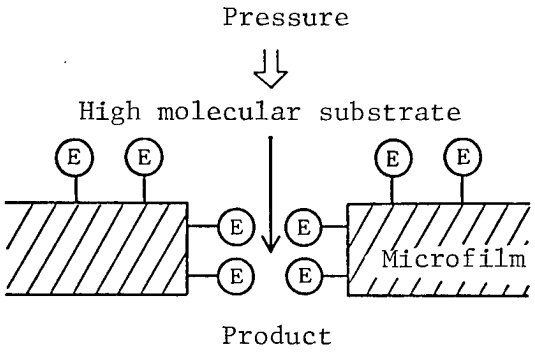

Figure 10. Enzyme Immobilized Membrane for Permeation and Hydrolysis of High Molecular Substrate

important factor, which has an overall control not only on the permeability of the enzyme immobilized membrane but also on its hydrolysis performance.

(3) Permeation and isolation type enzyme immobilized membrane

When the substrate is a low molecular compound, as in the case of continuously manufacturing invert sugar from sucrose, the sucrose can be hydrolyzed into glucose and fructose through an enzyme immobilized membrane as shown in Figure 11. Especially when sucrose needs to be hydrolyzed continuously in a high molecular solute mixture, an invertase immobilized membrane with separation functions is needed which enables the high molecular solute to be separated by the membrane and the sucrose to be hydrolyzed when passing through the enzyme immobilized membrane.

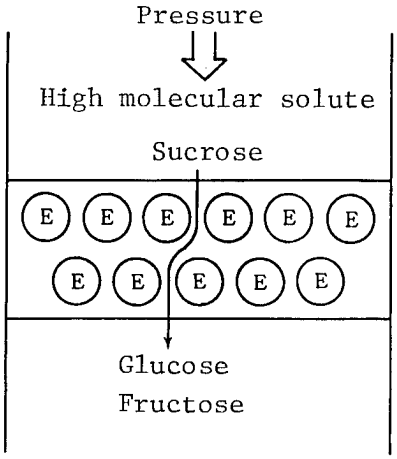

Figure 11. Permeation and Separation Type Enzyme Immobilized Membrane

Figure 12 shows the Lineweaver-Burk plot[15] of hydrolysis reactions of a sucrose solution when passing through an invertase immobilized membrane

which is prepared in the same way as an enzyme is immobilized in a polyion complex made from fourth grade chitosan and polyacrylic acid sodium, of which a description is given in paragraph 2.3.[42] When a water solution containing sucrose was passed through the invertase immobilized membrane, the sucrose molecules were almost 100 percent hydrolyzed. As shown in Figure 12, hydrolysis reactions of sucrose through the invertase immobilized membrane were quite similar to ordinary enzymatic reactions.

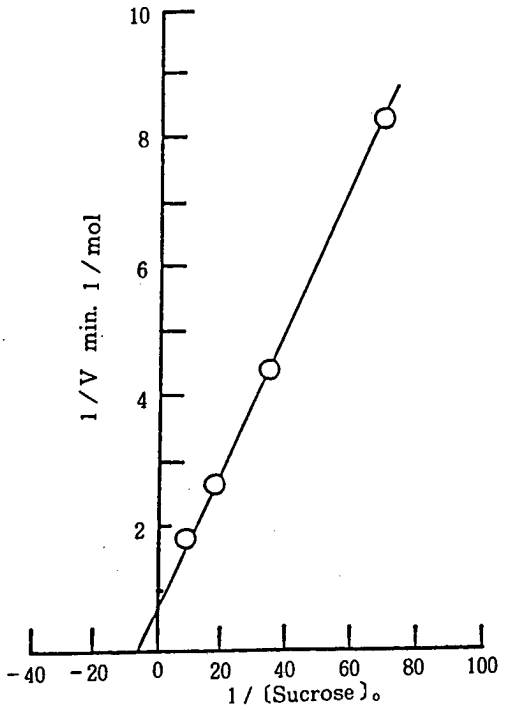

Figure 12. Lineweaver-Burk Plot in Hydrolysis of Sucrose in Invertase Immobilized Polyion Complex Membrane

The quantity of an enzyme to be immobilized in a polyion complex can be controlled to some extent by changing the quantity of the enzyme added to a fixed amount of cast solution when the membrane is grown. When the enzyme needs to be immobilized in a much larger quantity, the immobilizing membrane layer is made thicker by increasing the quantity of cast solution, which increases the hydrolysis capacity. But an increase in the thickness of a membrane causes the solutions to pass through it at a slower rate. Consequently, performance evaluation of an enzyme immobilized membrane will have to be based on multiplication of the hydrolysis rate and permeation speed.

(4) Membrane type reactor

Enzymes are used in two types of applications. One is the case in which an enzyme is immobilized inside a high molecular gel membrane or a high molecular support membrane, where the water-soluble enzyme is utilized as an enzyme insoluble in water. The other is the case in which, as shown in Figure 9(d),

an enzyme is confined in the solution contained on one side of an ultrafiltration membrane or a hollow fiber membrane, where the enzyme is expected to display the same capabilities when it is immobilized, and this is called the membrane type reactor.[3,49-51]

Depending on the shape of the membrane used, membrane reactors are classified into the following types, flat membrane reactor, tubular membrane reactor, hollow fiber membrane reactor, compound membrane reactor incorporating a semitransparent membrane and an enzyme gel layer, and microcapsule type reactor.[49]

The hollow fiber membrane developed for use in blood dialysis and ultrafiltration is impermeable to high molecular substances and has a large unit permeation area. The enzyme membrane type reactor takes advantage of these features. The reactor is a bundle of hollow fibers, with an inside diameter of 200 to 500 μm and an outside diameter of 300 to 900 μm, numbering from several thousand to 10,000-odd pieces, inserted and fixed inside an inner tube or tank-like vessel.[52] The enzyme is immobilized either inside or outside the tubing containing the hollow fibers membrane.

The substrate solution passes through the membrane from the opposite direction of the tube and shifts to the side of the enzyme solution, and products produced by enzymatic reactions pass through the membrane and are separated.

Since membranes used in this reactor come in various graduated molecular weights, selection of a membrane that selectively let a substrate on which an enzymatic reaction is needed pass through, will guaranteehigh efficiency reactions. The membranes are also of two types, symmetric and asymmetric, but symmetric membranes are not appropriate to use since their permeability resistance is great. Even asymmetric membranes are not fully satisfactory at present when used inindustrial applications. But, in the field of membrane science and industry, studies have recently been advancing on the technology of manufacturing ultrathin membranes in various fields, and ultrathin membranes usable in industrial applications are about to make their debut.[53] So, in the near future, an enzyme reactor based on an ultrathin membrane may be used industrially.

(5) Immobilization of enzymes by taking advantage of density polarization phenomenon

The use of an ultrafiltration membrane or a hollow fiber membrane in the processing of a high molecular solution usually leads to the formation of a gel layer on the membrane surface, lowering its efficiency.[54,55] This is a functional drawback of the membrane's permeability.

Attempts, however, have been made to actively take advantage of the density polarization phenomenon as a means of immobilizing enzymes onto the surface of polymeric membranes. Included, for example, are the formation of an enzyme gel layer by completely condensing an acid phosphatase water solution using a cellulose acetate membrane and an enzyme immobilized in a gel of high molecules made through density polarization in a mixture of the enzyme and water-soluble high molecules as an enzyme reactor.[58]

Such applications of membranes are not suitable for hydrolysis reactions of high molecular substrates, and they are effective in uses where the substrate can penetrate the gel-enzyme immobilized layer.

(6) New impregnation immobilization method

An interesting method[50] has been tried in which when the intensified active layer with separation functions in the hollow fiber membrane of the ultrafiltration type cannot fully block and separate enzyme molecules, the enzyme is permitted to pass through the layer, whereupon it is introduced into the porous layer with support functions on the outside for impregnation and immobilization. Impregnation of glucoamylase, an enzyme for saccharifying starch, and enzyme isomerization have been achieved by this technique. An examination of their activity revealed that the velocity of the flow running through the tube plays an important role.[59,60]

4.2 Applications to Analyses

Representative enzyme immobilized membranes are enzyme sensors, referred to as enzyme electrodes. Taking advantage of their excellent reaction specificity, enzymes have been used as reagents in analyses, and enzyme sensors are another instance where an enzyme's features are utilized as an identifying element of chemical substances. Enzyme electrodes represent the only case where enzyme immobilized membranes have been put to practical use. Many theories have been advanced on the subject[1,3,4,17,61-83] so the reader is referred to those references. In this paper, the importance of the separation function of enzyme immobilized membranes is described.

(1) Glucose sensor

Applications of enzyme electrodes in qualitative analyses owes its success in combining a glucoseoxidase immobilized membrane with an oxygen electrode.[83] That is, as shown in Figure 13, glucoseoxidase is contained and immobilized inside a membrane-like polyacrylamide gel; this enzyme immobilized membrane is placed on top of a synthetic polymeric membrane such as a teflon membrane that readily permits oxygen to pass through it but rejects water; the complex is combined with an oxygen electrode. When the oxygen electrode is inserted into a sample solution containing glucose, the glucose enters the enzyme immobilized membrane and diffuses. Then, a reaction takes place as shown in formula (11), consuming the oxygen, and the flow of oxygen to the oxygen electrode decreases. A measurement of the oxygen density at the oxygen electrode tells the quantity of glucose.

$$\text{glucose} + O_2 \xrightarrow{\text{glucoseoxidase}} \text{gluconic acid} + H_2O_2 \qquad (11)$$

Here, if the membrane that permits passage of oxygen but rejects a water solution could be made of the same membrane material as that for the enzyme immobilized membrane, the result would be a thin-filmed device, possibly leading

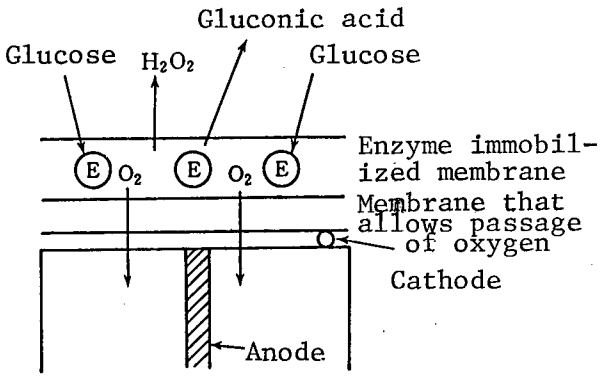

Figure 13. Example of Enzyme Sensor

to a shortened measurement time. In other words, as shown in Figure 14, when a carboxyl group is formed only on the membrane surface of a polyethylene thin film by surface oxidation, the film allows oxygen to pass through but refuses a water solution. This carboxyl group is turned into azide, chloride, isocyanate, or diimide derivatives, as shown in paragraph 2.1, and the required enzyme is immobilized by means of peptide bonds.

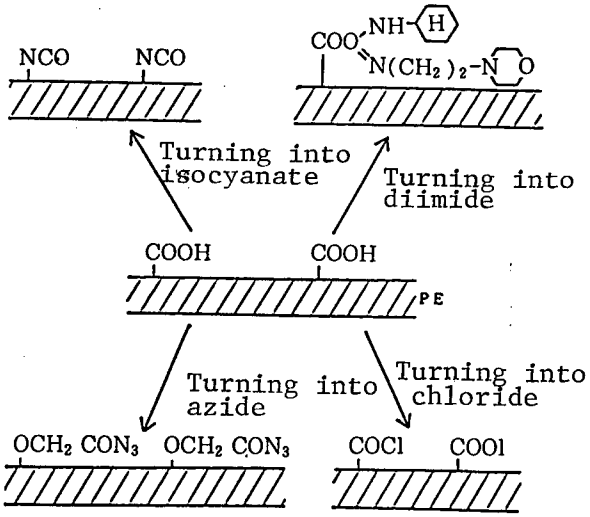

Figure 14. Activating Polyethylene Film Surface

(2) Alcohol sensor

In a sensor for measuring alcohol, either alcohol dehydrogenase or alcohol oxidase is immobilized onto a membrane, and either a decrease in oxygen or an increase in hydrogen peroxide, based on formula (12), is measured either at the oxygen electrode or at the hydrogen peroxide electrode.

$$R\text{-}CH_2OH + O_2 \xrightarrow{\text{alcohol oxidase}} R\text{-}CHO + H_2O_2 \qquad (12)$$

When using alcohol oxidase, if the sample solution contains organic acids, they are also oxidized. So, the correct quantity of alcohol cannot be measured. Even in such a case, the above problem can be solved by preparing an enzyme immobilized membrane as shown in Figure 14 and covering it with a cation exchange membrane, as shown in Figure 15, that blocks organic acids from passing through. Also, as shown in Figure 16, if one side of a water-insoluble cation exchange membrane is used as a polyanion and an enzyme is immobilized on the other side by a normal process, this prevents the organic acids from penetrating inside the membrane, and oxidation of only alcohol by the enzyme becomes possible.

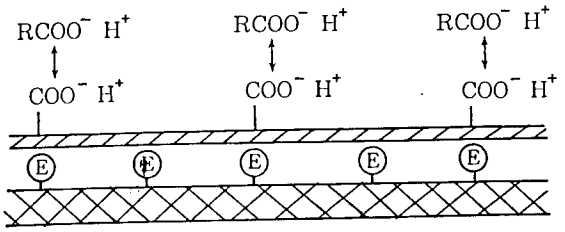

Figure 15. Ion-Selective Enzyme Immobilized Compound Membrane

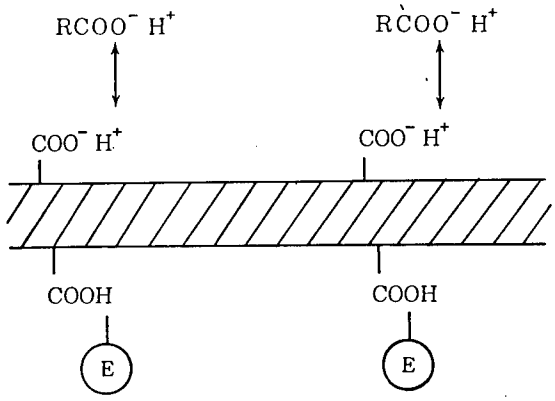

Figure 16. Ion-Selective Enzyme Immobilized Membrane

4.3 Applications in Medicine

One application area for enzyme immobilized membranes is their use in the medical field, and several studies have been undertaken.

4.3.1 Artificial Kidneys

Ordinarily, in artificial kidneys the blood and the dialysis solution are brought into contact across a dialysis membrane, and metabolites and water in the blood are removed by a passive transport. But with them, tasks shorten the time needed for dialysis and downsizing of the equipment.

(1) Microcapsule type enzyme immobilized membrane

With an objective of manufacturing small artificial kidneys, the idea of packing enzymes and activated carbon in microcapsules originated as early as the 1960s.[84] As shown in Figure 17, the idea is to use a microcapsule containing an immobilized urease in combination with a microcapsule containing activated carbon in order to adsorb noxious substances in the blood and remove them from the body.

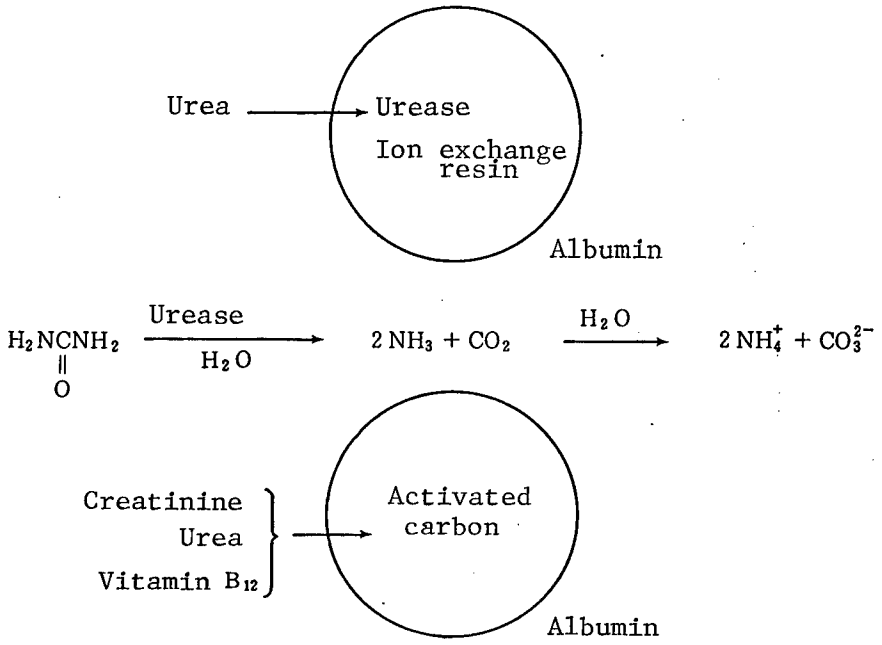

Figure 17. Microcapsule Type Enzyme Immobilized Membrane

Such metabolites as creatinine, uric acid, and vitamin B_{12} are relatively easily adsorbed by microcapsulated activated carbon and removed, but urea adsorbs only slightly to activated carbon. Therefore, urease, an enzyme that hydrolyzes urea, is immobilized inside a microcapsule, and an ion exchange resin immobilized inside the same capsule is used to adsorb and remove ammonium ions, products resulting from the decomposition of urea.

When these microcapsules are brought into direct contact with blood, thrombi are formed on the surface of the polymeric membrane. To prevent this from happening, the microcapsules have albumin adsorption-deposited on their surface.

On the other hand, when a urease immobilized microcapsule membrane containing an ion exchange resin is stuffed into a column together with activated carbon not microcapsulated and the column is connected to the dialysis side at the time of a blood dialysis, metabolites and urea flowing to the side of the dialysis solution are adsorbed and removed. This enables the dialysis solution

to be recycled for utilization, and compared with the conventional dialysis the new dialysis system enables the job to be done with a smaller volume of dialysis solution, thus opening the way for downsizing the equipment.

(2) Enzyme and adsorbent immobilized cellulose acetate membrane

With the above described microcapsulated enzyme immobilized membranes, it is possible to remove waste products in the blood, but it is not possible to remove water in the blood, which is another important function of artificial kidneys. Therefore, urease which is a hydrolase of urea, "styrite" (partial esterification product of an alternating copolymer of stylene and maleic acid anhydride) adsorbs ammonium ions and removes them, activated carbon which adsorbs waste metabolic products such as creatinine and vitamin B_{12}, and activated alumina which removes phosphoric acid ions have been immobilized into cellulose acetate membranes, and their ultrafiltration and adsorption characteristics have been studied under various conditions.[85-88]

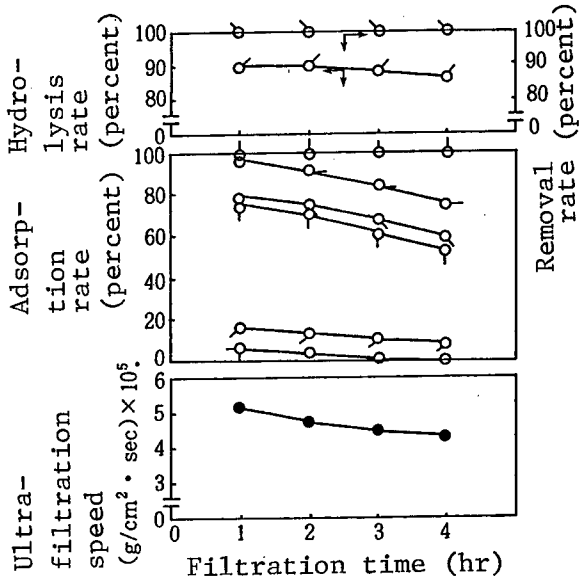

Figure 18. Model Blood Filtration and Adsorption Characteristics of Compound Cellulose Acetate Membrane Immobilized With Urease, "Styrite," Activated Carbon, and Activated Alumina

(♂) Urea; (♀) creatinine; (○) BSP; (♀) Vitamin B_{12}; (♂) KH_2PO_4; (○) NaCℓ; (○) NH_4^+ adsorption rate

Figure 18 shows the results of tests conducted using a water solution containing albumin, sodium chloride, urea, creatinine, BSP, and vitamin B_{12} as a blood model. The ultrafiltration speed drops with time. This is caused by such factors as clogging of the membrane pores, compaction of the membrane under pressure, and condensation and polarization of albumin molecules. Hydrolysis of urea is 100 percent completed, ammonium ions are removed 100 percent, and creatinine, BSP, and vitamin B_{12} are fairly well adsorbed. The

adsorption rate of Na^+, an electrolyte, on the other hand, is extremely low, while albumin molecules are completely removed.

Figure 19 shows blood filtration characteristics in tests conducted using bovine blood containing heparin. The ultrafiltration speed of cellulose acetate membranes immobilized with urease is about two times that of the "Caprofan" membrane for blood dialysis.

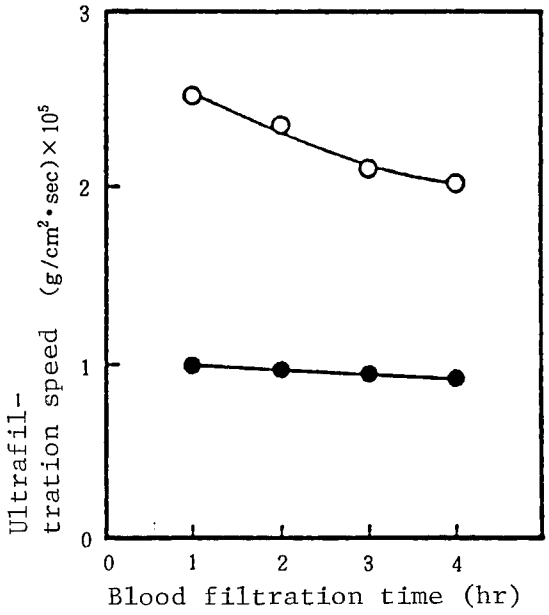

Figure 19. Bovine Blood Filtration Characteristics

o Urease, "styrite," activated carbon, compound cellulose acetate membrane immobilized with activated alumina
● "Caprofan" membrane
Filtration condition: 200 mmHg, 200 mℓ/min, 40°C

Table 5 shows the rate of hydrolysis and the rate of removal in filtration tests conducted using bovine blood. The rates for hydrolysis of urea and for ammonium ion removal are 100 percent, and the results are fully satisfactory for an enzyme immobilized membrane. The removal rate of phosphoric acid ions is a little bit low, but the adsorption of creatinine is fairly good. Albumin is 100 percent removed, and the separation function of the enzyme immobilized membrane is fully satisfactory.

This enzyme and adsorbent immobilized membrane with separation functions is effective against thrombosis.[89]

Table 5. Results of Analysis of Urea

Matter for filtration	Adsorption rate	
Urea	100[a]	100[b]
Creatinine	81.3	
BSP	96.6	
PO_4^{2-}	10.5	
N_a^+	6.3	
Albumin	100[c]	

a: hydrolysis rate; b: removal rate of NH_4^+;
c: removal rate

(3) Sandwich type enzyme immobilized membrane with separation functions

When blood is brought into contact with a cellulose acetate membrane immobilized with urease, etc., urea in the blood is hydrolyzed on both sides of the contact surface, which may raise the concentration of ammonium ions in the blood. In such a case, the sandwich type enzyme immobilized membrane with separation functions described previously is effective.

That is, lamination of a protective layer on top of the enzyme immobilized layer permits controlling of the reaction between urea and urease taking place in the vicinity of the interface between blood and membrane and at the same time prevents the products produced by enzymatic reactions inside the membrane from diffusing into the blood side.

(4) Membrane immobilized with various enzymes

A hibernating bear does not eat or drink, nor does it urinate. But the animal is not afflicted by urine poisoning.[90] This is because the metabolism mechanism of a bear in hibernation undergoes a change, which enables products produced in the process of protein metabolism to be reused inside the body, thus eliminating the need to discharge waste matter and water from the system. This has been confirmed by the fact that in a test tube the bacterium Micrococcus glutamicus turns urea and ammonia into L-glutamic acids.[91] As such, immobilization of strains of bacteria, besides enzymes, is also an interesting subject, but the reader is recommended to refer to references 1, 3, 92-96.

As with M. glutamicus, for the purpose of changing ammonia and urea in the blood into glutamic acids a system of membranes immobilized with various kinds of enzymes has been developed.[97] That is, as enzymes urease, dehydrogenase glutamate, and glucose dehydrogenase for NADHP reproduction are used, they are contained and immobilized inside a collodion membrane as a microcapsule. Immobilization of a plural number of enzymes enables a complex reaction to take place.

Attempts at turning a waste product into effective elements or manufacturing a useful product from a waste product have been conducted using immobilized enzyme systems,[98-100] but such attempts are scarce using enzyme immobilized membranes.

In cases as described in the previous article where enzymes are immobilized into a matrix of polyion complexes by the ultrafiltration method, different types of enzymes can be stacked in many layers. That is, when immobilizing enzymes into a polyion complex membrane, no organic solvents or bridging agents are employed, so the immobilizing condition does not have many constraints, enabling immobilization of several types of enzymes.

4.3.2 Membranes That Control Passage of Drugs

Figure 20 shows a glucose response membrane that is a combination of a membrane immobilized with glucose oxidase and a polymeric membrane containing a nicotinamide group.[106] That is, when glucose passes through the glucose oxidase immobilized membrane, hydrogen peroxide is produced by an enzymatic reaction. By the action of hydrogen peroxide, the nicotinamide group turns into an oxygen nicotinamide, swelling the polymeric membrane. When insulin is placed at the opposite side of the membrane, it is diffused and transported, shifting to the left side as the membrane continues to swell. As the degree of the membrane's swelling changes with the volume of glucose, the degree by which the insulin passes through is controlled.

Such membranes that control passage of drugs are also an interesting research theme from the perspective of enzyme immobilized membranes.

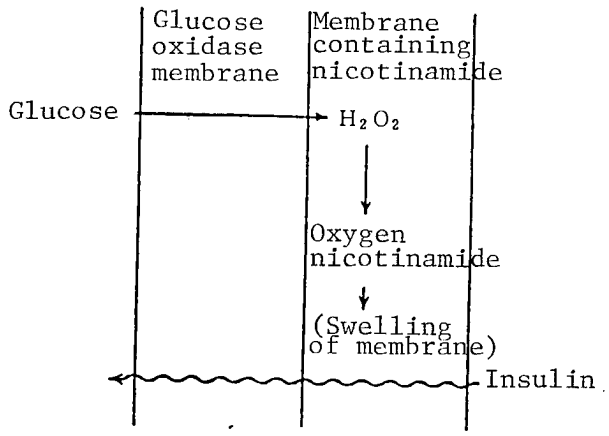

Figure 20. Glucose Response Polymeric Membrane[106]

4.4 Environmental Purification

Attempts have been made for utilizing enzyme immobilized membranes with separation functions for waste water disposal.

For example, when bleaching noodles, hydrogen peroxide is used, and the hydrogen peroxide and water-soluble starch contained in the waste water need to be treated. In such a case, the use of an ultrafiltration membrane immobilized with catalase and peroxidase permits the starch to be separated by the membrane and the hydrogen peroxide to be disintegrated when passing through the enzyme immobilized membrane, thus performing separation and disintegration simultaneously. As in this case where the solution to be processed is not so complex in nature, enzyme immobilization is advantageous from various perspectives. But running research on whether similar functions can be obtained with synthetic polymers not containing enzymes is also worthwhile. That is, it is to utilize characteristics of conventional ultrafiltration membranes for the separation of starch and to disintegrate chemically or physically hydrogen peroxide without using enzymes.

It is well known that polymer-metal complexes possess catalytic functions.[101-102] As for the hitherto announced catalysts based on polymer-metal complexes, however, they have almost invariably been used in solutions of uniform quality. Therefore, under the judgment that the essential point of the membrane is that it not only provides the forum for reactions but also possesses separation and transportation functions, membranes based on polymer-metal complexes have been prepared. For example, algic acid-copper (II) complex-based membranes[103] and polyvinyl alcohol-copper (II) complex-based membranes[104] are prepared as stable membranes insoluble in water. The disintegration and catalysis capabilities of these complex-based membranes against hydrogen peroxide are similar to the enzyme catalysis functions of catalase and peroxidase. Hydrolysis of p-nitrophenyl esters is possible since they can pass through those complex-based membranes.[105]

As such, membranes based on polymer-metal complexes have similar functions as enzyme immobilized membranes to some specific substrates. If it is possible to obtain the desired reaction without using expensive enzymes but instead cheap and easy-to-handle synthetic polymer systems, the field will be worth studying.

The cellulose acetate membrane immobilized with urease, "styrite," activated carbon, and activated alumina, described in paragraph 4.3, was developed for processing blood but it is also available for purification and treatment of dialysis solutions. Furthermore, it is effective for disposal of waste water discharges from medical facilities, and with proper selection of the enzyme, membranes immobilized with an enzyme and adsorbent may be effective for the treatment of waste water.

4.5 Application to Condensed Form Transportation

Figure 21 shows a model for active transportation of glucose through its condensation using an enzyme immobilized membrane.

When ion-selective membranes are placed on both sides of a complex membrane and a membrane immobilized with adenosine triphosphate (ATP) and hexokinase and a membrane immobilized with phosphatase are added between the two ion-selective membranes, glucose diffuses into the membrane from L side, is

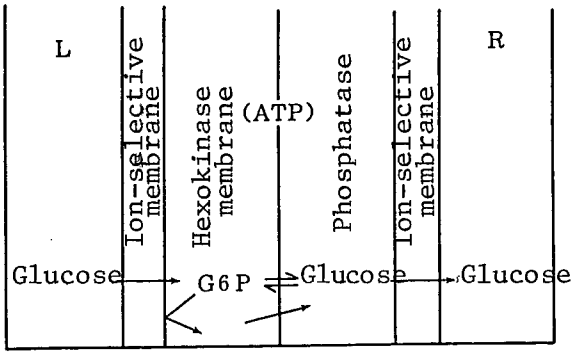

Figure 21. Active Condensation of Glucose Using Enzyme Immobilized Membrane

turned into phosphoric acid by the membrane immobilized with ATP and hexokinase, and is reduced to glucose-6-phosphate (G6P). The G6P is charged negative, and because of the electrostatic repulsion, it cannot pass through the ion-selective membrane. G6P, on the other hand, can diffuse into the phosphatase-immobilized membrane, where it is dephosphorized and turned into glucose for transportation to the R side. The transportation from the L side to the R side is an active one that occurs against gradients of glucose concentrations.[107]

The enzyme immobilized membrane shown in Figure 21 enables separation of mixed solutions of glucose and xylose,[109] and glucose and galactose.[110] That is, it takes advantage of the enzyme's substrate specificity that prevents xylose and galactose from turning into phosphoric acid. In this system, the problem is consumption of ATP as time passes, and the future task is how to supply ATP.

5. Future Prospects and Problems

5.1 Future Prospects

(1) Membranes as alternatives to fractionating columns in oil Kombinat

One dream application of polymeric membranes is their use as alternatives to fractionating columns in oil-refining facilities. Achieving this goal with the current membrane separation technology is yet impossible. But landing on the moon aboard a rocket was a big dream for ancient people. Man has already brought to reality this dream. In light of this fact, replacing fractionating columns with membranes in an oil Kombinat should not be laughed off as a pipedream.

(2) Production of alcohol from biomass

A dream at hand for enzyme immobilized membrane systems is their use in the production of alcohol from biomass. The applications of enzyme immobilized membranes with separation functions in the enzymatic reaction processes shown in Figure 22 lead to separation and reaction processes at high efficiency would be ideal.

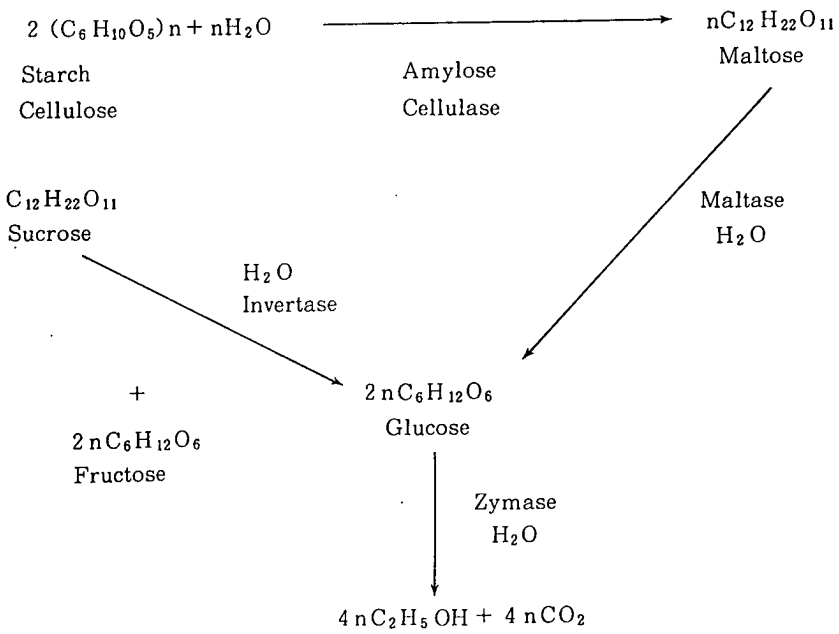

Figure 22. Production of Alcohol From Biomass

Needless to say, every enzymatic reaction process need not be done by means of an enzyme immobilized membrane, and combined use of simple immobilized enzymes and/or chemical catalysts should be considered. Great expectations are being held for the application of membranes immobilized with several types of enzymes, in addition to membranes immobilized with a single type of enzyme.

(3) Application to ocean development

The list of potential applications for enzyme immobilized membranes is long, but in the following their applications are described regarding development at the sea bottom.

Development of the ocean floor has been making strides in various fields, but the activity's importance is expected to further increase in the future. The key to ocean floor development is to create a condition where people can live with ease on the sea bottom. To that end, development of a membrane that permits oxygen to be taken in from the seawater and carbon dioxide to be discharged into it is necessary.

Such a membrane has been drawing attention for a long time for its use as an artificial gill. The polysiloxane membrane, for instance, enables oxygen to be taken in without letting water in. It, however, cannot easily discharge carbon dioxide. If an enzyme immobilized membrane is used, there is a possibility that the above function may be realized. That is, carbonate dehydratase is an enzyme that reversibly promotes the reactions as shown in formula (13).

$$CO_2 + H_2O \underset{}{\overset{\text{carbonate dehydratase}}{\rightleftharpoons}} H^+ + HCO_3^- \qquad (13)$$

When this enzyme is immobilized into a polymeric support membrane and is used in the state as shown in Figure 23, the reactions shown in formula (13) reverse, enabling carbon dioxide to be discharged from a room on the sea bottom.

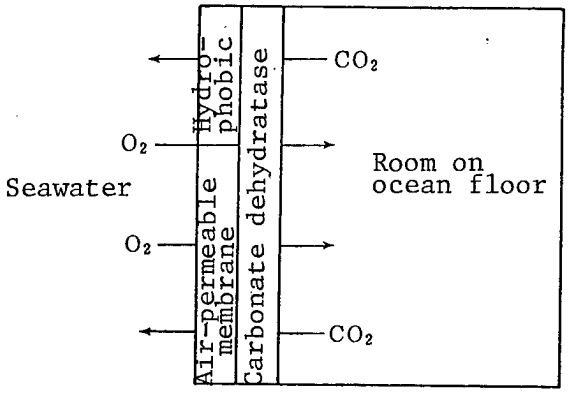

Figure 23. Potential for Application of Enzyme Immobilized Membranes to Rooms on Sea Bed

If such an enzyme immobilized membrane with separation functions is developed, it may find application in the membrane type lungs currently being used as artificial lungs. For oxygen inhalation, the artificial lungs of both the bubble and membrane types can relatively easily send oxygen into the blood by changing its partial pressure but they have problems with discharging carbon dioxide from the blood.

(4) Multistage reaction by membranes immobilized with several types of enzymes

At present, the world market for membranes and membrane technology is estimated at $150 million annually, but the scale is expected to increase to 10 times its current value in the 21st century.[110] As one of the developments, immobilization of specific enzymes onto membranes is drawing attention. Letting mixed airs or mixed solutions pass through an enzyme immobilized membrane stacked with several layers of different types of enzymes as shown in Figure 24 is expected to bring about a reaction which will take place in multistages because of the existence of the enzymes, to keep to a minimum side reactions, and thus generate smaller amounts of unnecessary products.

5.2 Problems

Many types of enzymes have so far been immobilized, and many basic studies have been made on them. But, only a small fraction of the immobilized enzymes have been put to practical use. In the field of enzyme immobilized membranes,

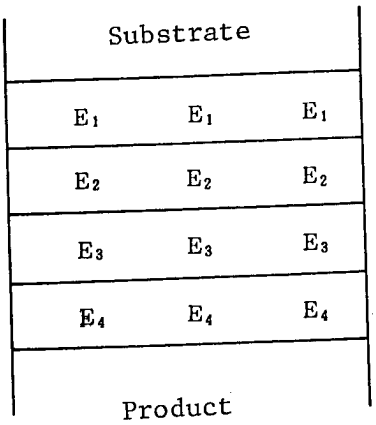

Figure 24. Membrane Immobilized With Several Types of Enzymes

in particular, only biosensors have been commercialized. The reason is because they cannot withstand repeated use over a long period of time.

Seen from the perspectives of enzyme engineering and membrane engineering, enzyme immobilized membrane engineering has problems as listed in Table 6.

Table 6. Enzyme Immobilized Membrane Engineering

Enzyme immobilized membrane engineering	Enzyme engineering Stability, heat resistance, solubility into organic solvent
	Membrane engineering Selectivity, thin-film membrane, morphogenic membrane

In enzyme engineering, the biggest problem is the stability of immobilized enzymes, and solution to the problem is awaited. Also, from the viewpoint of economics, the reaction speed needs to be raised. To that end, development of heat-resistant enzyme immobilized membranes, along with improvements on the immobilization method, is awaited. Furthermore, when fabricating an enzyme immobilized substance into a membrane from it is a great advantage if the substance dissolves into organic solvents. Development in this field is important and it is beginning to draw attention as protein engineering.

In the field of membrane engineering, on the other hand, development of a selective membrane that enables separation, that is, the capacity to isolate from a mixture of products produced as a result of reactions inside the enzyme immobilized membrane the required product from unnecessary byproducts, is awaited.

In order to obtain high-efficiency reactions and high permeability, an important factor is the technique of fabricating an enzyme immobilized membrane as a thin-film membrane, and the problem needs to be studied from both sides, enzyme immobilization and membrane growth. Furthermore, if enzyme immobilized membranes are to find practical applications, the absolute requirements are that they can be fabricated into a tubular or a hollow fiber type. So, R&D needs to be made on the technique that enables an enzyme immobilized membrane to be fabricated into a desired form.

The enzyme immobilized membrane technology has the potential that will make it possible to carry out reaction and separation functions in many of the systems where such capabilities were not available until now. With advances in research in various fields, the technology will find increasing applications in various fields. The science of enzyme immobilized membranes with separation functions astride a large number of disciplines including biology, microbiology, biochemistry, enzyme chemistry, organic synthetic chemistry, polymer chemistry, medical science, pharmacy, and chemical engineering, so an important task is how to implement cooperative research involving these diverse disciplines.

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INFORMATIONALIZATION POLICIES FOR FY87

Tokyo DENSHI KOGYO GEPPO in Japanese Feb 87 pp 2 - 12

[Article by Atsuki Ito, Electronics Policy Department, Machinery & Information Industries Bureau, Ministry of International Trade & Industry]

[Text] Introduction

Informationalization is proceeding apace in Japan, with the number of general-purpose (mainframe) computers installed now exceeding 200,000. The information-related industry as a whole has now grown to become Japan's leading industry, a 15-trillion yen industry that accounts for 4.8 percent of the nation's gross national product (GNP).

Needless to say, the advance of informationalization is fostering the rationalization of industrial activity, greater sophistication of industrial organization, and the intensive application of creative knowledge. It is also contributing largely to the realization of a better way of life for the people and to the enhancement of mutual understanding throughout the international community.

In order for the Japanese economy to continue to grow steadily in the medium and long term, not only must this information industry develop further, but informationalization must advance beyond the industrial fields to reach into our homes.

In a sense, the growth in the information industry and in informationalization thus far has been quantitative, while problems that are more fundamental and qualitative in nature are multiplying, so that we are now faced with the urgent need to appropriately deal with these fundamental and qualitative issues in order to realize the information society. In other words, we need to promote greater sophistication and improve the basic structures that support informationalization. More specifically, we need to upgrade information-related education and the training of data-processing technicians and other human resources, overcome our quantitative and qualitative software inadequacies, and move from intra-company systems to inter-company networks.

The Ministry of International Trade & Industry (MITI) will continue in fiscal 1987 to develop and promote comprehensive informationalization policies with a view to the above perspectives.

We will now give an overview of MITI's policies on informationalization.

1. Promotion of Information-Related Education, Human Resource Training

As informationalization progresses, the diversifying and increasingly sophisticated data processing needs in all industrial and societal fields must be met. In order to do this we must give urgent attention to the development of the human resources that support informationalization in these fields, and specifically to the actual use of computers in courses taught in our schools.

In fiscal 1987, MITI will promote a new information academy concept, and implement comprehensive information-related education and training programs.

(1) Information Academy Concept

In response to the shortage of software technicians, special schools and other information-related training facilities have sprung up rapidly, so that the arena of data-processing training is broadening. As a result, however, we are seeing increasingly wide divergence in the content of this training and in the qualifications of the instructors, leading to obvious problems in the qualifications of those being trained. Against this background, the information academy concept is being vigorously promoted in the dual interest of training superior data-processing specialists and invigorating regional information industries.

(A) Promoting Information Academy Concept

A central information academy will be established, research will be done on training methods, etc., for software technicians, and instructors will be trained for regional information academies. Regional information academies will be opened in various regions, training methods suitable to the needs of industry will be promoted with the cooperation of the regional academies, and regional data-processing training will be comprehensively improved.

<Budget> For promotion of information academy concept: 68 million yen (new)

Note: Amounts budgeted in fiscal 1986 are given in parentheses, as applicable.

Table Percentage of Those Passing Type II Data Processing Technician Examination

Classification	Fiscal 1985	Fiscal 1986
Graduate Schools	50.7%	63.0%
Universities	29.8%	30.1%
Special Schools	14.7%	10.3%
Average	20.9%	20.0%

(B) Courseware for Data-Processing Technicians (Development of CAROL System)

We are now faced with extreme inadequacies in terms both of the quality and quantity of our data-processing technicians (systems engineers, high-level programmers, etc.). Part of the information academy concept is to develop and widely implement software for training data-processing technicians according to the needs of industry.

Specifically, this involves the following three steps. (1) Establish the specifications for CAI (computer assisted instruction) systems (CAROL system) for training data-processing technicians. (2) Draft standard curricula for training data-processing technicians. (3) Promote the proliferation of the CAROL system.

<Finance> Industrial investment expenditure for development of software for training data-processing technicians: 600 million yen (new)

(2) Promoting Use of Computers in Schools

In today's world, with the rapid advances in informationalization, all levels of our population must be trained so that people will not be afraid to use computers and other information equipment (promotion of computer literacy). It is now being demanded that computers be abundantly employed in the school curriculum so that people will learn from childhood to treat computers as ordinary tools of life.

It is hoped, furthermore, that the use of computers in education will be an effective means of diversifying education methods.

From such perspectives as these, policies will be implemented, primarily through the Information Processing Promotion Association (IPA) and Computer Training Development Center, to promote the use of computers in our schools.

(A) Survey of Basic Data-Processing Technology for Use in Training

In order to promote the use of computers in school education, basic surveys will be done, and computers suitable for school use will be developed.

<Budget> For surveying basic data-processing technology for school use: 220 million yen (210 million yen)

(B) Development of Support Systems for Drafting of Training Materials

It is important that computer training materials (so-called courseware) adequately reflect the opinions of actual instructors. For this reason, development work will continue in fiscal 1986 on systems which support courseware development by instructors not accustomed to developing courseware.

This work will be done mainly through the Computer Training Development Center, which is jointly administrated by MITI and the Ministry of Education.

<Finance> Funds for promoting information-related training and human-resources development: 600 million yen (400 million yen)

2. Promoting Comprehensive Software Policy

The steady supplying of good software is a necessary condition for the realization of the information society. The demand for software, however, is currently growing explosively with the rapid advance of informational-ization, i.e. the rapid proliferation of computers. This software demand now grows at a rate of about 26 percent a year. Meanwhile, we have come to face a chronic shortage of the data-processing technicians who work to develop and produce software, with their number growing only at about 13 percent a year. Thus the demand/supply gap is becoming broader and broader, and it is even feared that this trend may become irreversible. In addition, the percentage of data-processing costs contributed by software-related expenses is becoming steadily larger, while greater software reliability and product quality are being demanded, making the software development situation very difficult.

For these reasons, IPA--the central promotional organization for software policies--will implement a comprehensive software policy, continuing to aggressively promote the Sigma project and seeking to actively use the Program Reserve System that is essential to making programs generally useful.

(1) Information Processing Promotion Association Operations

The following operations will be conducted, beginning with work to implement the software production industrialization system (Sigma system) that was begun in fiscal 1985 to rapidly improve productivity and reliability in software development.

(A) Creation of Software Production Industrialization System (Sigma Project)

<Finance> Industrial investment expenditure: 2.9 billion yen (2.8 billion yen)
Japan Development Bank financing: 500 million yen (300 million yen)

(B) Promotion of Program Development and Distribution

<Finance> Industrial investment expenditure: 1.5 billion yen (1.4 billion yen)

(C) Promotion of Information-Related Training, Human-Resources Development

<Finance> Industrial investment expenditure: 600 million yen (400 million yen)

(D) Low-Interest Financing of Program Development for Systems Jointly Used by Multiple Companies

<Finance> Government guaranteed loans: 1.8 billion yen (1.5 billion yen)

(E) Information Processing Promotion Association--General Accounting

<Budget> Information Processing Promotion Association operating expenses: 1.34 billion yen (1.26 billion yen)

(2) Data-Processing Advancement Funding (Japan Development Bank Funding)

Both capital and non-capital items will be financed for the automation of software development, training of software development specialists, and development of inter-company data-processing systems.

The most favorable interest rates of Special Rate 5 (6.05 percent as of January, 1987)--and for some items Special Rate 4 (6.10 percent as of January, 1987)--will be applied.

<Finance> Informationalization promotion bracket: Within 86.5 billion yen (Within 85.0 billion yen)

(3) Extension of Program Reserve System (Partial Expansion)

Making programs more general-purpose is an effective way to reduce the investments in program development in the society as a whole, and constitutes an immediate measure for dealing with the software crisis.

However, there are high developmental risks associated with developing general-purpose programs, and such programs will not be widely used if they are merely made available. Accordingly, the General-Purpose Program

Development Reserve System was established in 1979. This system has been promoting the development of general-purpose programs.

Along with the Program Maintenance Guarantee Reserve System that was established in 1972 to normalize company accounting procedures pertaining to free maintenance, the periods (for this and the aforesaid reserve system) will be extended for 2 years and the software policy will be continued.

In 1987, moreover, the Database Creation Reserve System will be newly established to promote the creation of databases.

(Reference) Overview of Program Reserve System

(A) General-Purpose Program Development Reserve

30 percent of the sales of general-purpose programs registered with IPA are placed in the reserve (reckoned as a loss)

(B) Program Maintenance Guarantee Reserve

0.22 percent of the sales of programs covered by a free maintenance warranty (reckoned as a loss)

(C) Database Creation Reserve

10 percent of sales pertaining to databases (reckoned as a loss)

(D) Left standing for 4 years in each case, then amortized on a straight-line basis over 4 years (reckoned as profit)

3. Assuring System Compatibility, Promoting OSI

As networking develops toward higher sophistication, the problem arises of how to mutually connect all the various and diverse information-handling equipment and systems. There is increasing user demand, moreover, for interconnecting different types of computers into networks.

In order to cope with these developments and promote interconnection between disparate computers, the OSI-related standardization work must be continued. There is also an urgent need for private-sector-based OSI work to be carried on by computer makers and end users.

MITI will continue to support these activities in the private sector as well as promote government-based international linking.

(1) Promoting OSI Through International Linking

(i) Implement high-level talks between Japan and EC pertaining to OSI promotion; implement government-based international linking, including holding talks among specialists.

(ii) Promote mutual linking among the private-sector OSI promotional organizations such as POSI (Japan), SPAG (EC), and COS (United States).

(2) Work Toward Implemnting Tests for OSI-Compatible Products

The Information Processing Interoperability Technology Association (INTAP) is doing studies on conducting compatibility tests on OSI compatibility for information-processing equipment. A test center will be established in fiscal 1987 and the work on implementing the tests will be intensified.

(3) R&D on Computer Interoperable Database System

Various different databases are now being operated which cannot be interconnected. Users who need various kinds of information now have to operate different terminals connected to the different databases, and the data accessible thereby are inadequate, being limited to text and graphics.

Thus there is a demand for a multi-media database system that comprehends all the different types and structures. A system will be researched and developed which can resolve all these problems at once.

With respect to OSI, (i) OSI-compatibility subsets and functional standards will be drafted, and (ii) verifications and evaluations are to be performed using a model system.

<Budget> Research and development of computer interoperable database system (large project): 1.06 billion yen (830 million yen)

(4) Promoting Advanced, Flexible Standardization of Information Technology Through JIS Activity, Etc.

Based on the results of studies done by the International Standards Organization (ISO), the OSI standards will also be established with Japan Industrial Standards (JIS).

4. Optimizing Industrial Informationalization

The industrial fields have been the driving force in pioneering the informationalization of Japan's economic society, and it is now necessary to implement informationalization that transcends the boundaries of businesses and industries by creating inter-industry networks.

For this purpose, the necessary facilities for promoting inter-industry networks will be put in place, and the informationalization of individual industries will be carried on while making use of the "Guidelines for Linked Utilization of Computers." In order to optimize the informationalization base, moreover, investment funds for computer promotion will be employed, and the computer repurchase loss reserve system will be extended.

Furthermore, realizing that industrial and societal activity depends strongly on information networks, the "Computer System Safety Standards" have been presented, places of business have been authorized to implement the safety measures for information processing service businesses and computer systems, and the "System Inspection Standards" have been presented, but safety measures must continue to be promoted.

(1) Computer Promotion Financing (Japan Development Bank Financing)

Financing will make available the necessary capital to conduct computer rental operations. The applicable interest rate will be Special Rate 5 (6.05 percent as of January, 1987) for the first 3 years, then Special Rate 4 (6.1 percent as of January, 1987) from the 4th year on.

<Finance> Within the 86.5 billion yen framework for informationalization promotion (within 85.0 billion yen)

(2) Financing for Promoting Data Processing, Communications Systems (Japan Development Bank Financing)

Funding will be provided for the capital and non-capital goods needed to set up systems, and database-building corporations will be funded, for the purpose of promoting the introduction of advanced, high-level information processing and communications systems, in responding to the needs of industry and society that are diversifying and becoming more sophisticated as informationalization advances.

The systems envisioned here are: (1) online data processing systems used jointly by multiple companies, (2) online data processing systems acquired by data processing services and information services, (3) socially significant systems such as those involving medical services, transportation, and disaster control, (4) so-called VAN and information-processing CATV operations, (5) videotex systems, and (6) region-promoting data processing and communications systems (new media communities).

A financing system has been established since fiscal 1986 for corporations that build basic databases and offer them for public use.

Moreover, beginning in fiscal 1987, financing will be recognized for non-capital funding for the systems noted above in (1), (2), and (3), and financing will be provided for the new media communities ((6) above), both for capital equipment and software development.

The applicable interest rate will be Special Rate 4 (6.1 percent as of January, 1987) (partially reserve rate).

<Finance> Within the 86.5 billion yen framework for informationalization promotion (within 85.0 billion yen)

(3) Funding for Improved Reliability of Information Equipment, Etc. (Japan Development Bank Funding)

Essential to the advanced information society is the realization of marked improvements in the reliability and performance of information-related equipment, components, and materials. Funding will therefore be provided for capital investments that pertain to improving reliability in manufacturing information equipment, etc.

The applicable interest rate will be Special Rate 5 (6.05 percent as of January, 1987).

<Finance> Within the 86.5 billion yen framework for informationalization promotion (within 85.0 billion yen)

(4) Government-Guaranteed Loans Pertaining to Low-Interest Financing by Information Processing Promotion Association

Government guarantees will be made available for loans of funds used as sources of low-interest financing provided by the Information Processing Promotion Association for the design of systems and development of software pertaining to information systems used within an industry or jointly between different industries.

<Finance> Government guaranteed loans: 1.8 billion yen (1.5 billion yen)

(5) Extension of Computer Repurchase Loss Reserve System

In acquiring computers, the rental approach is advantageous for users because (1) the installation costs are no more than 1 month's rental fees, and (2) it is easy to update equipment models to prevent obsolescence, etc.

On the other hand, it is difficult for computer makers to implement the rental approach, because (1) little revenue is provided by the provision of the computers, and (2) enormous capital is necessary in order to conduct rental operations, etc.

For this reason, the JECC-based rental system has been put into operation. With the mechanism employed here, however, the sales conducted between JECC and the makers contain repurchase agreements, so that repurchase losses are inevitably suffered when there is a rent-back.

The Computer Repurchase Loss Reserve System that makes allowances for these losses will be extended through fiscal 1987 in order to promote normalization of the manufacturers' corporate accounting.

(Reference) Summary of Computer Repurchase Loss Reserve System

(A) When there are losses connected with computer repurchases, a prescribed percentage of the sale price of the computer covered by a repurcase

agreement is accounted as a reserve (loss), according to the performance ratio therefor.

(B) When repurchase losses occur, they will be amortized (accounted as profit) sequentially, on an FIFO basis.

(6) Promotion of Intra-Industrial Informationalization

For individual industries that are important in terms of influencing regional informationalization and other industries, informationalization will be studied on an industry-by-industry basis, and "linkage indexes" will be established, based on the "Law Pertaining to Promotion of Information Processing."

5. Promotion of Development of Information Technology

In order for Japan's economic society to achieve a powerful, high-level information society, and respond to the diverse industrial and societal needs, it is essential that technological development continue to be promoted.

To this end, intense efforts will continue to be made in fiscal 1987 toward researching and developing the fifth-generation computer that is crucial to the advance of informationalization, researching and developing computer interoperable database systems, developing high-speed computer systems for science and technology, and developing advanced social systems.

Efforts will be made to aggressively utilize the financing functions of the Key Technology Center, and to promote research and development at R&D companies formed with funding from this center.

(1) Fifth-Generation Computer R&D

With an eye to the 1990's, great efforts will continue to be made in researching and developing a new generation of computers that will employ such revolutionary technologies as artificial intelligence, high-level informationalization, and parallel processing.

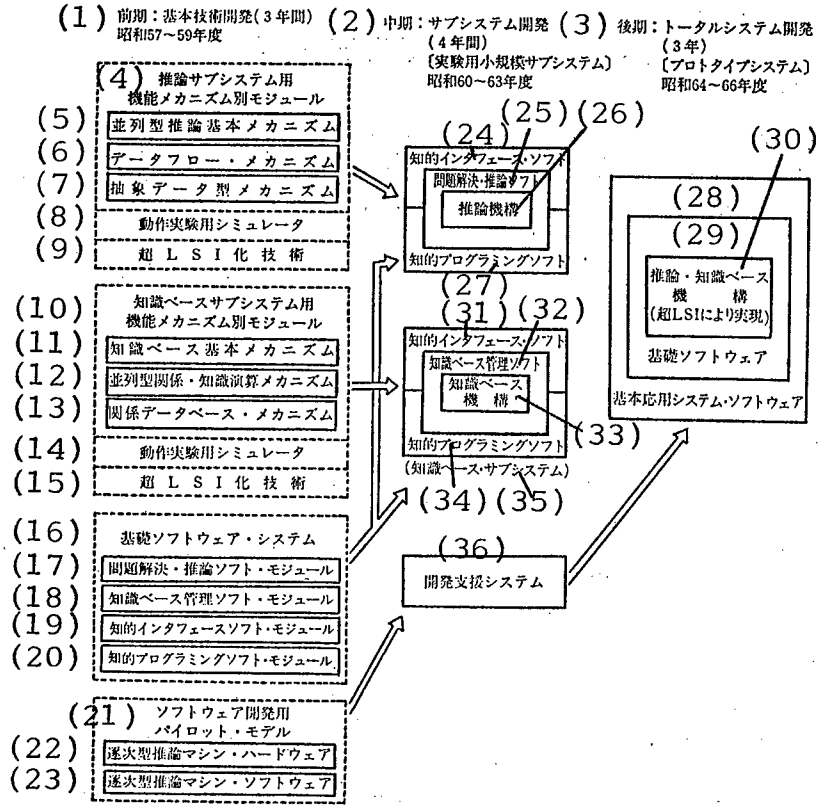
In fiscal 1987, which is the third year of the middle period, work will be done on the design of partial systems in order to implement logic subsystems and knowledge base subsystems, etc. (Cf. Figure 3)

<Budget> General accounts, special accounts: 5.63 billion yen (5.49 billion yen)

(2) Computer Interoperable Database System R&D (Large Project) (Noted above)

<Budget> General accounts, special accounts: 1.06 billion yen (830 million yen)

Figure 3 Fifth-Generation Computer--R&D Steps



Key:

1. Initial Period: Develop basic technology (3 years), fiscal 1982-1984
2. Middle Period: Develop subsystems (4 years) (small experimental subsystems), fiscal 1985-1988
3. Final Period: Develop complete system (3 years) (prototype system), fiscal 1989-1991
4. Modules for each functional mechanism for logic subsystems
5. Parallel logic, basic mechanisms
6. Data flow mechanisms
7. Abstract data mechanisms
8. Simulator for operational tests
9. VLSI-based technology
10. Modules for each functional mechanism for knowledge base subsystem
11. Knowledge base, basic mechanisms
12. Parallel-processing related knowledge & computation mechanisms
13. Relational database mechanisms
14. Simulator for operational tests
15. VLSI-based technology

16. Basic software system
17. Problem solution, logic software modules
18. Knowledge base management software modules
19. Intelligent interface software modules
20. Intelligent programming software modules
21. Pilot model for software development
22. Sequential logic machine hardware
23. Sequential logic machine software
24. Intelligent interface software
25. Problem solution, logic software
26. Logic structures
27. Intelligent programming software
28. Basic application systems software
29. Basic software
30. Logic, knowledge base mechanisms (VLSI implemented)
31. Intelligent interface software
32. Knowledge base management software
33. Knowledge base mechanisms
34. Intelligent programming software
35. (Knowledge base subsystems)
36. Developmental technology systems

(3) R&D on High-Speed Computing System for Science & Technology (Large Project)

Research and development work will continue on high-speed computing systems in which the computational speed has been dramatically increased, i.e. on systems which can be used for scientific and technological computations such as the processing of image data received from weather satellites.

<Budget> General accounts, special accounts: 2.95 billion yen (2.89 billion yen)

(4) Bioelement R&D (Part of R&D System for Next Generation Industries)

Serious R&D work will begin in order to elucidate the information processing functions found in living organisms and implement bioelements, i.e. electronic devices which adopt these high-level functions.

<Budget> 150 million yen from the budget for R&D on new-function elements (60 million yen)

(5) Development of Diagnostic Support Systems

In order to raise the level of medical practice and make medical treatments more effective through promoting informationalization in the medical field, work will be continued in developing consulting systems designed to directly support physicians in making diagnoses.

<Budget> General accounts, special accounts: 170 million yen (100 million yen)

(6) Activities of Key Technology Center

The Key Technology Center functions to promote experimental research on basic technology in the private sector by distributing the necessary risk money.

In fiscal 1987, financing--including conditional, interest-free financing--will be made available to corporations conducting joint experimental research and to corporations that promote the new-media community concept, and efforts will be made to promote joint research at national research facilities, thereby continuing to promote technological development through the Center.

<Finance> Investment operations: 17.3 billion yen (12.5 billion yen)
Financing operations: 7.7 billion yen (5.7 billion yen)

6. Building Informationalized Futuristic Cities

In the interest of promoting growth in domestic demand as well as the realization of the advanced information society, it is necessary to accelerate informationalization investing in industry, society, and the home.

In this interest, a field will be established for creating advanced information systems that can be employed in special model cities going into the 21'st century. By moving ahead with the creation of a network system that will comprehensively advance informationalization in each field, this will be made a priming agent for implementing greater proliferation of information systems in society.

In fiscal 1987, intense efforts will be made to build informationalized futuristic cities by implementing new budgetary, financing, and tax measures.

<Budget> For implementing social-development-type mechanized information systems: 60 million yen (new)

<Finance> For maintaining international-information-type regional- development base facilities--
Japan Development Bank financing: Within 171.0 billion yen (new)
Hokkaido-Tohoku Development Fund financing: Within 135.0 billion yen (new)

<Tax System> Add international-information-type regional-development base facilities to the New Industry Society Basic Facility Maintenance Investment Promotion Tax System.
(A) Add 20 percent special depreciation to regular depreciation for first year of acquisition.

(B) Implement tax-reducing measures on fixed-asset taxes, etc., for regional taxes as for other civic facilities.

7. Promotion of Regional Informationalization

In order to smoothly implement the high-level information society, it is essential that the differences in informationalization between the regions be corrected, and that balanced informationalization be promoted throughout the country.

To this end, the development of new media communities will be promoted in the regions with the objectives of developing various information systems, and implementing their proliferation, according to regional needs. Other means of promoting regional informationalization will also be implemented, such as maintaining regional informationalization base facilities and employing fiscal measures to promote regional informationalization.

(1) Developing New Media Communities Into Applications Development Regions

Regions which have adopted model information systems and developed them will be designated as new media community concept applications development regions, and feasibility studies will be conducted.

After the model information systems that are set up in the model regions have been made to conform to standard specifications, they will be equipped with database facilities, and further regional informationalization will be promoted by employing these systems in similar regions.

<Budget> General accounts: 50 million yen (60 million yen)

(2) Promoting Maintenance of Regional Informationalization Base Facilities (New Media Centers) Based on Civic Activity Law

In order to promote the maintenance of regional informationalization base facilities (new media centers), which are expected to play a central role in regional informationalization and contribute to the development of regional industry and economy, a system for financing the construction of these facilities through the Japan Development Bank and Hokkaido-Tohoku Development Fund will be established.

<Finance> Regional Informationalization Base Facility Maintenance--
Japan Development Bank financing: Within 171.0 billion yen (new)
Hokkaido-Tohoku Development Fund financing: Within 135.0 billion yen (new)

(3) Regional Informationalization Promotion Financing (Hokkaido-Tohoku Development Fund Financing)

The problem of the regional discrepancies in informationalization must be resolved in response to the needs of the regions that are diversifying and

becoming more sophisticated as informationalization advances. In order to do this, funding will be provided to finance the capital and non-capital expenditures needed to build systems for promoting the introduction of advanced and sophisticated data processing and communications systems.

The systems envisioned here are: (1) online data processing systems used jointly by multiple companies, (2) online data processing systems acquired by data processing services and information services, (3) socially significant systems such as those involving medical services, transportation, and disaster control, (4) so-called VAN and information-processing CATV operations, (5) videotex systems, and (6) region-promoting data processing and communications systems (new media communities).

Moreover, beginning in fiscal 1987, financing will be recognized for non-capital funding for the systems noted above in (1), (2) and (3), and financing will be provided for the new media communities ((6) above), both for capital investments and software development.

The applicable interest rate will be Special Rate 4 (6.1 percent as of January, 1987) (partially reserve rate).

<Finance> Within 135.0 billion yen framework for regional development (within 135.0 billion yen)

(4) Regional Informationalization Base Facility Maintenance Financing (Hokkaido-Tohoku Development Fund Financing)

In order to address the software crisis with a multi-pronged strategy and respond to the regional software development demand, funding will be provided for industries that undertake software development in the Hokkaido-Tohoku region, including the provision of capital for plant and equipment and long-term operating funds.

The applicable interest rate is Special Rate 2 (6.15 percent as of January, 1987).

<Finance> Within the 135.0 billion yen framework for regional development (within 135.0 billion yen)

(5) Financing of New Media Community Concept Promoting Corporations by Key Technology Center

In order to promote the new media community concept even more strongly, funding will be provided by the Key Technology Center to corporations that promote this concept.

<Finance> Within the 17.3 billion yen financing framework of the Key Technology Center (within 12.5 billion yen)

8. Constructing Databases, Upgrading Information Services

Together with hardware, software, and human resources, databases constitute one of the main pillars that support the information society, and the preparation of databases is a precondition for informationalization. Japan is far behind many foreign countries, however, in the construction and maintenance of databases, and there is a pressing need to catch up.

In order to promote database operations in Japan, a comprehensive database promotion policy will be implemented, including promoting database creation in the private sector, promoting the construction of public databases, nurturing distributors, and providing government-held data to the public.

<Budget> Construction and promotion of database and information services: 84 million yen (76 million yen)

(1) Promoting Construction of Critical Databases

A developmental and planning survey will be conducted with a view to constructing databases that are critical to the development of Japan's economy, in such fields as advanced technology (fine ceramics, new materials, etc.), energy, and security.

(2) Promoting General International Database Distributors

A survey will be conducted to determine the societal and technological needs and the form that such business should take should a system of general international distributors be set up to handle database distributors and producers. Another survey will be conducted concurrently on the software, etc., needed to make database retrieval easy and efficient.

(3) Surveys Related to Database, Information Services

Surveys will be conducted to determine the needs, both on the supplier and user sides, involved in database, data retrieval, and video-audio information services, and to make specific policies for constructing, maintaining, and promoting such services.

(4) Creating Public Databases, Expanding Availability of Government-Held Data

The creation of public databases (technology, patents, small-business related, etc.) necessary to the implementation of MITI administrative policies will be continued. These databases will be made widely accessible to the private sector and the conditions for accessing them will be determined.

(5) Supporting Database Creation in Private Sector

Japan Development Bank funding will be made available to corporations that create basic databases needed for the future development of industry and societal activity, and both capital and non-capital financing will be provided for businesses that create databases.

In order to reduce the burden involved in constructing and updating databases, moreover, a new database creation reserve will be established.

(A) Financing Database Creation (Japan Development Bank Financing)

Non-capital funding will be provided to corporations conducting information services for the equipment and preparation costs incurred in creating databases.

The applicable interest rate will be Special Rate 4 (6.1 percent as of January, 1987).

<Finance> Within 86.5 billion yen framework for promotion of information-alization (within 85.0 billion yen)

(B) Financing for Corporations Building Basic Databases (Japan Development Bank Financing)

Financing will be provided by the Japan Development Bank to corporations involved in information services which build "basic databases" necessary for the development of industrial and societal activity and of regional society.

<Finance> Within 86.5 billion yen framework for promotion of information-alization (within 85.0 billion yen)

(C) Establishing Database Creation Reserve

A reserve system will be established wherein, with the capital necessary for database creation and updating treated as a reserve, 10 percent of sales will be included in this reserve (counted as a loss), left standing for 4 years, and then amortized (counted as a profit) on a straight-line basis over the next 4 years.

(6) Establishing Database Register

Work will continue on setting up a database register that includes the type, location, and content of the various databases which can now be used in Japan.

9. Cooperating in Informationalization in Developing Nations

In order to promote the international development and growth of informationalization, active cooperation will continue to be extended to the developing nations, particularly to those in the Pacific basin.

(1) Cooperative Research on Machine Translation Systems Among Neighboring Nations

In order to promote technological and cultural exchanges between the nations that are close neighbors of Japan, and promote further development in those nations, serious work will begin in cooperative research to develop machine translation systems aimed at resolving the language barriers between Japanese and the other languages. These systems will translate between Japanese, on the one hand, and the Chinese, Thai, Malay, and Indonesian languages, on the other.

<Budget> From the budget for research cooperation, promotion, and support operations, and cooperative research operations: 170 million yen (30 million yen)

(2) Promotion of International Informationalization Center Operations

Research will be conducted on training technicians for the purpose of promoting informationalization in order to contribute to the economic and industrial development of the developing nations, and technicians will be dispatched from Japan to these nations to provide guidance in implementing informationalization.

<Budget> From the budget for subsidizing technological cooperation operations: 240 million yen (240 million yen)

(3) Surveys on Information, Communications Infrastructures in ASEAN Countries

The current status of information and communications facilities in the developing nations will be analyzed to determine the roles played by information and communications in the local economies and the needs for sophisticated information and communications systems. Based on these findings, policies will be developed with the local governments on establishing industrial infrastructures to support the implementation of sophisticated information and communications technology.

<Budget> Within 120 million yen for comprehensive development and planning survey operations (90 million yen)

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MASS PRODUCTION, FURTHER USES EXPECTED OF SHAPE-MEMORY ALLOY

Tokyo NIKKO MATERIALS in Japanese Nov 86 pp 14-18

[Article by Takeo Matsuoka]

[Text] New materials is considered on the the three pillars of high-technology. In recent years, among new materials, a shape-memory alloy has been applied to leisure equipment and industrial products, and has advanced to a stage in which it will soon be mass produced. The metal with the unique characteristic of memory has been recognized in the market, and has been used in various fields such as electrical appliances, automobile parts, robots, etc. And, considering the unique function of this metal, there is the prospect that the metal will be developed further. This article will explore the future course of the shape-memory alloy which will soon be mass produced.

The shape-memory alloy is a new metallic material that possesses a characteristic known as "reversibility of deformation." That is, when a test piece whose shape is fixed constantly at a certain temperature is deformed at a lower temperature and then later is returned to the original temperature, it will spontaneously regain its original shape.

The most typical deformation of usual metallic materials is plastic deformation. This is a permanent deformation. In order to return usual metallic materials which have been deformed plastically to their original shapes, it is usually necessary to apply external force to them. On the contrary, the shape-memory alloy can be deformed without any plastic deformation. In addition, this operation can be carried out repeatedly. The shape-memory alloy is really a metal with memory.

It is advisable to make the best of this unique characteristic of the shape-memory alloy. During the past several years, experiments on application of the shape-memory alloy to new industrial functional materials have been conducted enthusiastically, and application examples have been introduced in various fields. Of course, metallic manufacturers have been keeping a watch on this high marketability, and have enthusiastically been participating in the field of this new metal.

Cooperation in Advancing the Use of Shape-Memory Alloy in the Future

The ERASMA (Engineering Research Association of Shape-Memory Alloys) has considered that in order to widely use the shape-memory alloy in various fields such as mechanical parts, medical materials, etc., in the future, it is necessary to carry out the research and development of this new metal. Six main manufacturers concered with the new metal have carried out the technical research and investigation work under the sponsorship of MITI since October 1983. The ERASMA has kept its organization as an association, but has completed the technical research work for the present, because the application of the Industrial Activation Technical Research and Development Cost Subsidy System expired at the end of this March. The ERASMA has decided to undertake publicity for the shape-memory alloy in the future.

Six companies, the Furukawa Electric Co., Ltd., Tohoku Metal Industries, Ltd., Daido Steel Co., Ltd., Sumitomo Special Metals Co., Ltd., Mitsubishi Metal Corp., and the Dowa Mining Co., Ltd. are manufacturers which have joined the ERASMA. The research theme of these companies is as follows: The Furukawa Electric Co., Ltd.: Unidirectional shape-memory alloy based on nickel and titanium; Tohoku Metal Industries, Ltd.: Bidirectional shape-memory alloy based on nickel and titanium; Daido Steel Co., Ltd.: Shape-memory alloy based on nickel and titanium according to a powdering method; Sumitomo Special Metals Co., Ltd.: Shape-memory alloy based on copper, aluminum, and beryllium; Mitsubishi Metal Corp.: Unidirectional shape-memory alloy based on copper, zinc, and aluminum; and the Dowa Mining Co., Ltd.: Bidirectional shape-memory alloy based on copper, zinc, and aluminum.

The first purpose of the establishment of ERASMA is to establish a technology for manufacturing the high-performance and high-reliability shape-memory alloy at a low cost. The main research theme up to now has been "Improvement of Elements." The shape-memory alloy must be manufactured by enhancing the temperature accuracy in the case where this alloy is returned to its original shape so that it has little deviation at a temperature change specified by users. Also, a method of designing elements such as number of turns of springs, etc., must be established by improving shape-memory characteristics such as the amount of repeated strain.

Another research theme is the life of shape-memory alloys in the case where they are heated or cooled repeatedly. For the time being, shape-memory alloys based on nickel and titanium must withstand 1 million heating and cooling cycles, and those based on copper must withstand 10,000 heating and cooling cycles. Also, research on high-performance shape-memory alloys has been conducted with the aim of reducing the cost by using a special manufacturing method (use of powder, etc.).

ERASMA has prepared investigative data on the new metal and has taken up research activities. In 1984 and 1985 ERASMA issued the "Patent Investigation Report on Shape-Memory Alloys" and the "Bibliography Investigation Report on Shape-Memory Alloys," respectively. In 1986 ERASMA will issue the "Element Design Manual" as well as the "Special Investigation Report on Shape-Memory Alloys." This manual will be issued as a part of the

business fiscal year report; it will cover abundant data on shape-memory alloys and will be useful for users.

Tsutomu Isobe, chief director of ERASMA and executive director of the Furuka Electric Co., Ltd. said, "We will continuously carry out various kinds of works for spreading the shape-memory alloys, and we will prepare manuals for announcing the contents of patented products." He said, "We succeeded in realizing the anticipated result, and we will promote the spread of shape-memory alloys in the future." Naturally, he predicts a bright future of these shape-memory alloys.

The delivery period of subsidies for ERASMA is about 2 1/2 years, about half that for other associations because some shape-memory alloys have been adopted in actual products such as eyeglass frames since ERASMA was established. In other words, these shape-memory alloys are at a stage which is ahead of the experimental stage but behind the mass-production stage.

Large Number of New Participants

Enterprises which are presently developing the shape-memory alloys are steel and nonferrous metals manufacturers such as Kanto Special Steel Works, Ltd., Kobe Steel, Ltd., Sumitomo Electric Industries, Ltd., Sumitomo Metal Mining Co., Ltd., Nippon Stainless Steel Co., Ltd., Nippon Steel Corp., etc., as well as the above six companies which have joined ERASMA. Also, with regard to national and public research institutions, the National Research Institute for Metals of the STA (Science and Technology Agency), the Mechanical Engineering Laboratory of the AIST (Agency of Industrial Science and Technology), the Osaka Prefecture Industrial Research Institute, etc., are conducting the research and development of the shape-memory alloy by using original manufacturing methods.

Of the above companies, the Furukawa Electric Co., Ltd. is the first company which has conducted research and development of the shape-memory alloy with interest. It was in 1963 that the company started research on shape-memory alloys based on nickel and titanium. Although the company lagged behind other companies in the discovery of shape-memory effects, it was several months ahead of U.S. companies in the patent (in Japan) of the composition of these shape-memory alloys based on nickel and titanium. The nickel-titanium alloy is a metal which has come into the limelight as a structural material excellent in corrosion and wear resistances, and has been manufactured and sold as a structural material for chemical plants. The company has led the industrial world in shape-memory alloys by making the best of the above experience and manufacturing know-how as shape-memory effects come into the limelight. It has almost dominated the domestic market, has shipped samples to more than 300 companies, and has delivered mass-produced products in about 10 out of the 300 companies.

The Furukawa Electric Co., Ltd. set about research and development of shape-memory alloys in 1963, and began full-scale application of these shape-memory alloys to various fields on a full scale by starting the sale of the Furukawa Shape-Memory NT Alloy and the Furukawa Super-Elastic NT Alloy in April 1980. In this year the company started delivering the super-elastic NT alloy wire

and the shape-memory alloy wire for heat engines, etc., in Suwa Seikosha Co., Ltd. (now, Seiko Epson Corp.) and Sharp Corp., respectively. The number of inquiries reached several hundreds.

It was in 1982 that the company took a mass-production system for shape-memory alloys by taking advantage of an opportunity that the company started delivering the NT alloy wire (memory processed product) for toys in Takara Co., Ltd. A product to which shape-memory effects are applied, was put to practical use and was put on the market for the first time in September of this year. It is a driving source for opening and closing a shutter of a dry unit of a full-automatic electronic drying storehouse jointly developed by Toyo Living Co., Ltd. and Kato Hatsujo Co., Ltd. A shape-memory alloy spring in which the critical temperature is set, is used to close the shutter between the storehouse and side room. The cost can be reduced to one third that of machines employing a conventional opening and closing electromagnet, and about 10 percent of the power consumption can be reduced.

Promotion of Application of Shape-Memory Alloys to Electrical Appliances

The shape-memory alloy has been recognized in the industrial world since it was applied to full-automatic electronic drying storehouses. In 1983 large electric manufacturers, Sharp Corp. and Matsushita Electric Industrial Co., Ltd., commercialized a new microwave oven and a new hot and cool air-conditioner, respectively. A shape-memory alloy spring is incorporated in a driving source for opening and closing a ventilating damper of the new microwave oven and in a wind direction deflecting mechanism of the new room heating and cooling air-conditioner, respectively.

Electrical appliances employing a shape-memory alloy have been appearing. For example, an electric coffee mill can employ such a new metal in the temperature sensor and driving unit; a bathroom basin hot water washer uses new metals in a valve closing mechanism. The temperature indicator of electromagnetic cooking equipment also employs such metals.

Of course, interest in the shape-memory alloy is not limited to the electrical appliance industry. Actually, shape-memory alloys are used in various fields such as space development unit, energy relevant equipment, automobile, machinery, medical equipment. The lunar surface or artificial satellite antennas, solid-state engines, water drain valve for steam air heating and conditioning, engine clutch overheating prevention devices, circuit connectors, optical fibers for communication, pump for artificial kidneys, contraceptive appliance, all employ new metals.

Akimitsu Satoh, section chief of Planning Department of Development Division of the Furukawa Electric Co., Ltd. has promoted the research and development of shape-memory alloys in the company. He said, "In particular, the automotive industry has recognized the shape-memory alloy. This is all the more meaningful because the world attaches importance to reliability. In addition, the shape-memory alloy has become well known in general because it is used in brassieres."

Shape-Memory Alloys Enhance Reliability in Automobiles

With regard to the shape-memory alloy used in automobiles, MMC (Mitsubishi Motors Corp.) adopted a shape-memory alloy in the automatic switchgear of fog lamp covers in 1982, and Toyota Motor Co., Ltd. adopted such a new metal in the abnormal sound proofing unit of manual speed gears in 1985.

Shape-memory alloys were used around the engine of automobiles for the first time in this summer. Toyota Motor Co., Ltd. and Aisin Seiki Co., Ltd. have jointly developed a fuel evaporation gas exhaust inhibiting unit employing a shape-memory alloy with a view to smoothly driving an engine and to smoothly starting automobiles equipped with the engine, and have actually incoporated it in these automobiles. This unit is designed so that it can make a charcoal canister absorb gasoline steam generated from gasoline in a float chamber by the atmospheric temperature rise of a carburetor, can prevent an air inlet system from being in an excessively concentrated condition, and can raise the restarting capacity. A shape-memory alloy is used in a control valve which is an important section of the unit, and when the atmospheric temperature of the carburetor reaches a constant temperature, the control valve will be opened or closed. As described above, the shape-memory alloy has been adopted in the main mechanism of engines, which needs the high-temperature reliability and the high-durability. Therefore, it is expected that the function and quality of shape-memory alloys will be highly evaluated and the demand for these shape-memory alloys will increase.

Large Demand for Shape-Memory Alloys for Brassieres

Another product which has greatly contributed to the increase in demand for shape-memory alloys is a brassiere with a shape-memory alloy, announced by Wacoal, Inc., in February. The unit demand for brassieres is the highest product demand. There are few products employing a shape-memory alloy in total amount of more than 1 ton. However, the total amount of shape-memory alloys used in brassieres will probably exceed 2 tons. New materials frequently are being used in fields which could not have been envisaged at the time they were developed.

Up to now, stainless steel or similar material has been used as a wire in brassieres in order to mold the female body line. But, such brassieres are often judged to be uncomfortable. They have the further disadvantage of bending during cleaning and permanently altering their original shape. Therefore, brassieres with a shape-memory alloy have come into the limelight. The most flattering shape of breasts at a temperature of about 25 degrees centigrade is memorized in a shape-memory alloy, and the shape-memory alloy is used in brassieres. When such a brassiere is put on a breast, the breast can be kept beautifully, because the shape-memory alloy is used in a wire which follows the curve of the breast. That is, such shape-memory alloys have a shape-memory effect and a super-elastic effect which causes metal to become soft like rubber. Brassieres with a shape-memory alloy have become very popular among women since being marketed in February. The number of brassieres sold annually has exceeded the 600,000 expected at first. The company will sell 700,000 brassieres with a shape-memory alloy during the six

month period up to July, and is contemplating extending its brassiere business to the United States.

The largest demand for shape-memory alloys at this time is for brassieres. It seems that this situation will continue for the time being, but it is expected that shape-memory alloys will be used increasingly in the fields of robots, medical equipment, etc., in the future. Also, the application of shape-memory alloys to thermal engines with no power source is another research theme.

The application of shape-memory alloys to robots is a theme which will be studied soon worldwide. Actuators with a shape-memory alloy are compact, lightweight, and flexible.

Actuators convert various energies into mechanical energy, and enable robots and automatic machines to begin a movement. That is, these actuators play the leading role, and take movements which are almost the same as those of human muscles. For example, School of Science and Engineering of Waseda University, the University of Electronic-Communication, and Hitachi, Ltd. have developed a bio-muscle type micro-manipulator, a biped locomotion robot, and a three-finger robot, respectively. The Furukawa Electric Co., Ltd. has developed a five-finger robot arm by working a shape-memory alloy in the shape of tape which is different from that of conventional round wires. As a result, this kind of robot can have a maximum of 17 degrees of freedom, a compact mechanism, and high-speed driving motions. In addition, it can take motions similar to those of human muscles, because it has 17 degrees of freedom (14 degrees of freedom in fingers and 3 degrees of freedom in wrists) in total, and it is operated by electro-conductively heating a shape-memory alloy incorporated in it.

Greater Application of Shape-Memory Alloys to Medical Fields Expected

On the other hand, it can be expected that a large amount of shape-memory alloys will be used in dental correcting wires. The Furukawa Electric Co., Ltd. and Tomy International Inc., a dental material manufacturer have jointly developed a new dental correcting wire, and began marketing it this February. This is the first time that shape-memory alloys have been put to practical use in the medical field. Up to now, stainless wires have been used in orthodontics. Force necessary for correcting the dentition can be applied continuously to teeth in accordance with the degree of progress of care, because the shape of wires at a temperature of about 37 degrees centigrade in the mouth is memorized by the shape-memory alloy. Also, compared with stainless wires, shape-memory alloy wires have the advantage of causing no problem in replacing or adjusting them and are excellent in corrosion resistance. Therefore, these shape-memory alloy wires have the high-safety and little elution of nickel during their use.

It is said that the number of orthodonic patients is around 100,000 in Japan; it is anticipated that the demand for shape-memory alloys will continue to increase, because of the common practice of orthodontics in the West. Therefore, it is expected that the West and Japan will become large markets for shape-memory alloys.

The application of shape-memory alloys to energy equipment (heat engine) can be cited as another noticeable market. The heat engine can effectively convert a large amount of low-quality energy discharged from it into mechanical or electrical energy. This matter has gradually come into the limelight. The heat driving engine employs a shape-memory alloy as an energy converting element. Shape-memory alloys will probably be used to replace the nuclear fusion reactor core which is an original energy source with a new one.

The Furukawa Electric Co., Ltd. overwhelmingly dominates the market for mass-produced goods employing shape-memory alloys. The company explains that they have a long history resulting from continuous efforts to use the applied knowledge. A company official said, "The demand for shape-memory alloy will not increase unless other companies aggressively follow us in the field of shape-memory alloys." Tohoku Metal Industries, Ltd., a competitor of the company has commercialized several products such as simple-type fire alarms, joints, etc., employing a bidirectional shape-memory alloy with the durability equivalent to that of unidirectional shape-memory alloys under the condition in which the deformation amount is about 2 percent. Also, Daido Steel Co., Ltd., and Nippon Stainless Steel Co., Ltd. specializing in the production of lamellar alloys are developing the shape-memory alloy. It will not be very long before products employing a shape-memory alloy are put on the market.

The shape-memory alloy possesses unique characteristics, but as it is a typical "seeds-type" material, it had been behind the others in the application work. At last, the period of the use of shape-memory alloys has come into the expansion stage. If the shape-memory alloy can be seen as useful in everyday goods, its future in mass production is assured.

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PROMOTION OF BASIC, ADVANCED RESEARCH DISCUSSED

S&T Themes

Tokyo PUROMETEUSU in Japanese May 86 pp 10-14

[Article by Policy Planning Office, Planning Bureau, Science and Technology Agency]

[Text] With the marked progress in science and technology [S&T] both in the nation and abroad recently, there are rising S&T expectations from technically innovating industries and their new developments in society.

The Science and Technical Council has reported the "Science and Technology Policy Outline," basically on our nation's future S&T policies to the Prime Minister on 3 December 1985. In this outline, the promotion of creative S&T is raised as a step forward towards the 21st century. It especially stresses the promotion of basic and initiative S&T.

1. Japan's S&T Structure and New Policy Development

Looking at the postwar S&T development of our nation, technologies such as environmental pollution prevention technology after 1965, resources and energy conservation technologies of the latter part of the 1970s and electronic technologies of the early part of the 1980s have been developing their own individual courses. These technologies are based on advanced technical standards from the latter part of the 1950s to the first half of the 1970s owing to the introduction and absorption of the latest technologies of the Western nations and expansion of science and engineering related personnel.

However, in general, technology progress is mainly enforced by the private sector, as shown in Table 1, which indicates that approximately three-fourths of the research and development [R&D] in Japan is conducted by this sector. 1) The incentives by the private sector and technologies demanded by the users for high technical standards (such as semiconductor manufacturing, fermentation techniques) are strong, and 2) large-scale, basic or initiative technologies with high risks (such as artificial satellites, aircrafts), or 3) economically inefficient technologies which require long-term steady efforts as well as accumulation of experiences such as management of genetic resources or basic software are relatively weak, and the nation seems unable to fully make up for this weakness as a whole (Table 2).

Table 1. Governmental Share in Research Expenses of Major Nations

Nation	Fiscal year	Government share
Japan	1982	23.6 percent
Japan	1983	22.2 percent
United States	1983	46.0 percent*
Great Britain	1981	47.7 percent
West Germany	1983	42.3 percent
France	1983	57.8 percent

Note 1: *represents estimated value.
2: Japan's governmental share concerns natural science field only while the shares of other nations are the total of natural science, humanities, and social science fields.
3. Source from FY 1985 Edition, S&T White Paper

Table 2. Comparison of U.S.-Japan S&T Standards and R&D Ability

S&T Standards

	R&D Ability: United States leads	R&D Ability: Equal footing	R&D Ability: Japan leads
Japan leads		Industrial robots Semiconductor manufacturing Fermentation technology	Magnetic levitation train Copying press
Equal footing	Machine translation Machine tool	Semiconductor IC Large scale computer Ocean energy Solar thermal power generation	Artificial heart Housing construction
United States leads	Gene recombination Chemical safety assessment Civil airplane Robots	Coal liquefaction Stock and crops control R&D of medical products	

Source: Research by S&T promotion coordination fee, "Comprehensive Analysis of S&T Standards and R&D Potential"

While the private sector will continue to play a great role in the nation's R&D activities, the government must voluntarily promote basic and initiative R&D fields which cannot expect full enforcement by the private sector. It is also necessary for the nation to complete environmental conditions to further activate R&D activities of this sector.

As our nation's S&T policy, there is report No 11 or "Basic Policy of S&T Promotion Over a Long-Term Perspective To Cope With New Situational Changes" from the Scientific and Technical Council, submitted in November 1984. This report was prepared to be the basis of S&T promotion for the coming 10 years, based on three principles: 1) promotion of original S&T, mainly in the basic and initiative fields; 2) harmonious progress between S&T, man and his society; and 3) S&T policy with emphasis on international circumstances.

The government has been enforcing various measures to realize this report by the Scientific and Technical Council. In July 1985, the Extraordinary Administrative Reform Promotion Council pointed out that the policy outline to promote Japan's S&T efficiently and preponderantly should be decided by a Cabinet council in its report on "Plans To Promote Administrative Reform." Consequently, a question was asked by the Prime Minister to the Scientific and Technical Council regarding the "S&T Policy Outline" (hereinafter referred to as Policy Outline). The council held deliberations based on the contents of report No 11 and the S&T situation since then and settled the report on 3 December 1985. This Policy Outline will become the basis for S&T promotion policy at the administrative level and is expected to be settled by the Cabinet council by this March. Thus, an S&T policy will be positioned as a priority policy of the national level which has great significance for us aiming at becoming an S&T nation.

2. S&T Policy Outline and Its Background

The Scientific and Technical Council's report on the "S&T Policy Outline" is composed of three parts, namely, "I. Basic Plan," "II. Promotion of Priority Measures," and "III. Promotion of Important R&D Fields."

I. Basic Plan

The Policy Outline places the promotion of S&T, mainly original S&T as the basic plan which demands policy measures to focus on basic and initiative R&D.

In other words, Japan must create the seeds of technologies which return to fundamental principles and phenomenon and promote original S&T which surpasses the frame of mere remodeling of revision in future R&D, in order to construct an affluent society for the 21st century and make subjective contributions to the world in S&T fields.

Our nation's weaknesses in the basic and initiative fields which are often referred to as the characteristics of Japan's S&T, are clearly shown, for example, in the different number of theses printed in major international magazines specializing in the latest technologies, between Japan and the United States (Figure 1). This is also fully understandable due to the extremely low Nobel Prize winners from Japan (Table 3).

Table 3. Comparison of Nobel Prize Winners by Nations

(Unit: percent)

Nation \ Period	Entire period	1901-1918	1919-1945	1945-1983
West Germany	14	31	22	6
France	6	18	7	3
Great Britain	16	15	20	16
Subtotal	36	64	49	24
United States	38	5	19	53
Japan	1	-	-	2
Others	25	31	32	21
Total number of winners	359 (100 percent)	55 (100 percent)	86 (100 percent)	218 (100 percent)

Note: Sum of physics, chemistry, medicine, and physiology related prize winners.

Source: FY 1984 Edition, S&T White Paper

Under these circumstances, the Policy Outline sets its central concept to the promotion of basic and leading S&T.

Furthermore, the Policy Outline instills "harmony between S&T, man and his society," and "emphasis on the international situation" which are indicated in report No 11 of the Scientific and Technical Council as items to fully consider when promoting S&T policies.

Thus, items for promoting basic and initiative S&T have been clarified with consideration to the increasingly closer relations between S&T, man and society as seen in the advancement of life science or the information society and greater recognition of S&T as a common asset of all mankind.

II. Promotion of Priority Measures

In the basic plan of the Policy Outline, completion of R&D systems and promotion conditions are raised as the common basic policy for every R&D field.

(1) Completion of a Promotion System

Our nation's R&D has proceeded in the past, with universities taking over academic research while national research institutes, etc., conduct R&D with administrative necessity and private enterprises carry out R&D directly resulting in practical usage. However, the role of the respective research organs is changing in accordance with R&D trends such as lengthening the R&D term by private enterprises (time required for self-developed technology to become practically applicable: 2.35 years in 1963 → 3.54 years in 1985, according to S&T White Paper 1985). Consequently, the Policy Outline states that universities should strengthen research activities to meet the social demands

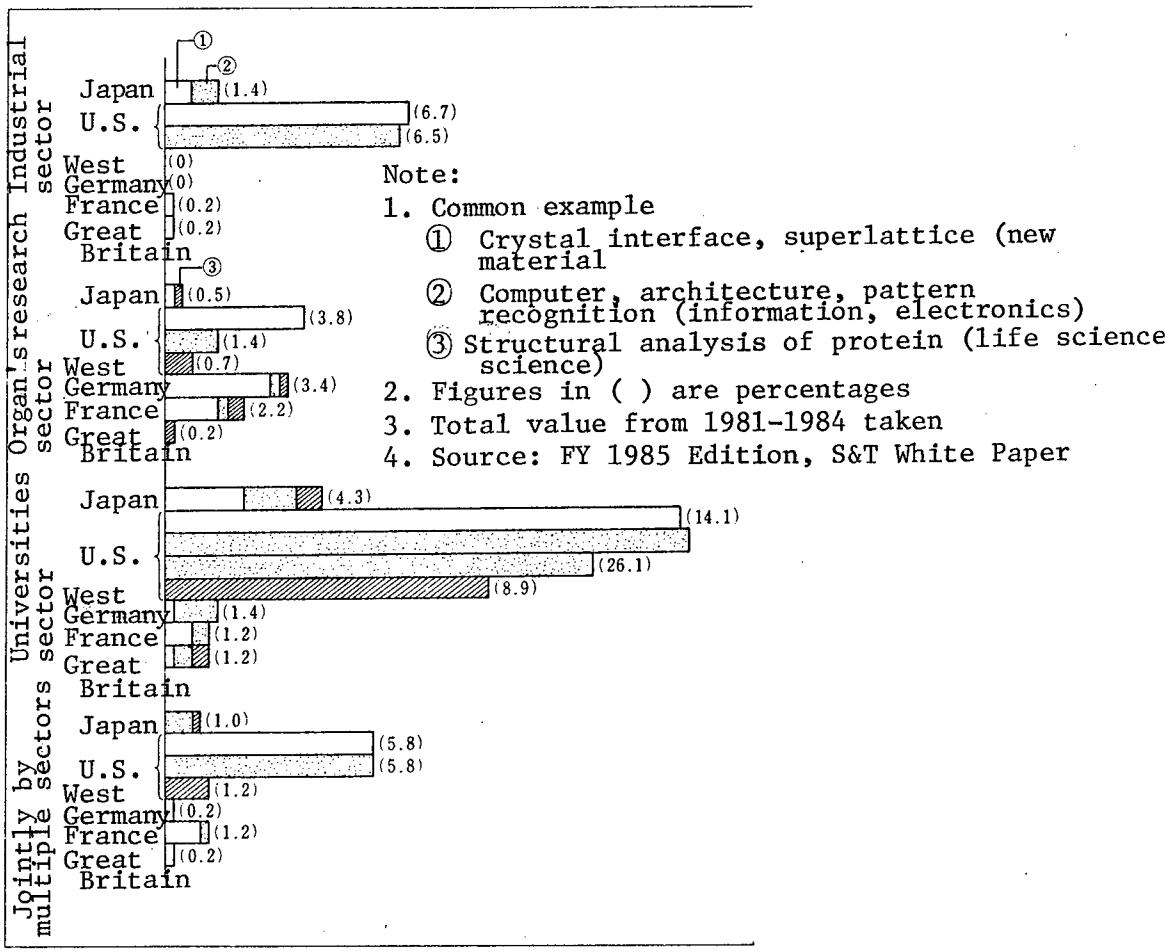


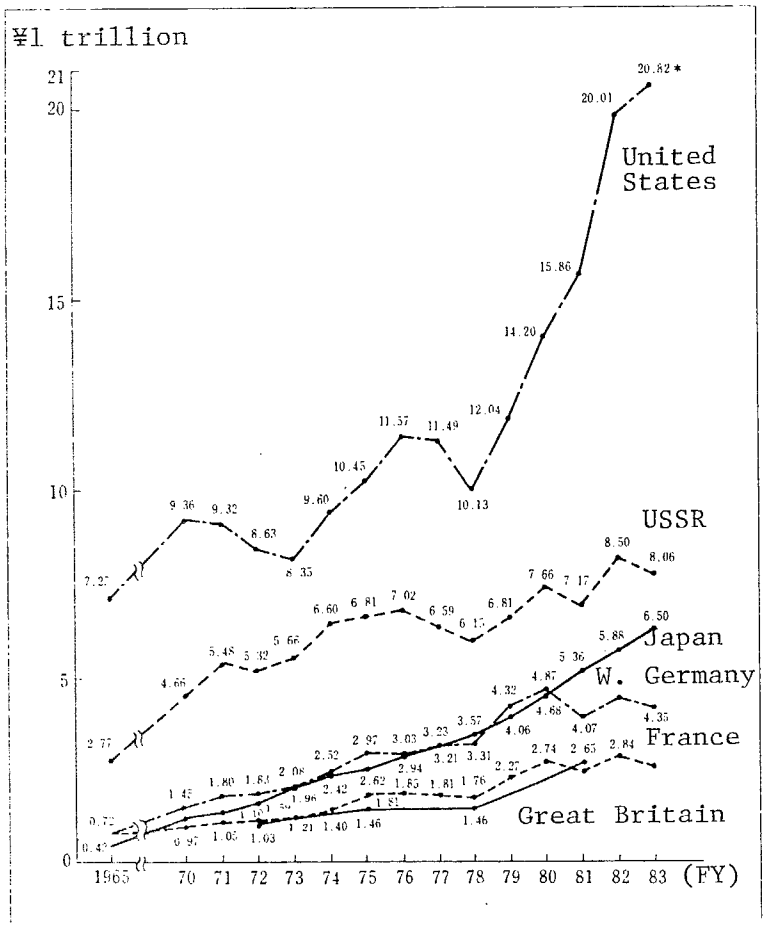
Figure 1. Comparison of Theses of Five Leading Nations Printed in Major Magazines

while assuming their mission and object in academic research. As for national research institutes, etc., basic R&D which will lead to original technologies for future generations and initiative R&D which draws out development of wide-ranging S&T fields should be stressed. Moreover, it urges us to revise the system and make its management flexible from the standpoint of promoting research exchanges between industries, academic organs, and governmental institutes.

Middle- to long-term plans for the future to activate national research institutes will also be fully examined by the Scientific and Technical Council.

(2) Completion of Promotion Conditions

The Policy Outline also indicates the course of R&D environmental problems such as investments, personnel, and foundations required for R&D promotion.



Note:
1. Japan's figures only concern the natural science field, while the applied figures of other nations also include humanities and social science fields, except for FY 1981 of Great Britain which only accounts for the natural science field.
2. *represents estimated value.

Source: FY 1985 Edition, S&T White Paper

Figure 2. Change in Research Expenses by Nations

1) Expansion of R&D Investment

The R&D expenses of our nation as a whole are ¥7.2 trillion (FY 1984, Figure 2) which amounts for 2.29 percent of the national income. Report No 11 of the Scientific and Technical Council suggests that R&D expenses invested by the government and the private sector as a whole should be 3.5 percent over the national income. The Policy Outline seeks to complete conditions for R&D investment both by the nation itself and by private enterprises towards this goal.

2) Training and Securing Talent

Training and securing talent such as researchers and technicians are basic items in the promotion of S&T. Thus, it is important to gather researchers, etc., both in quality and in quantity. The extremely few personnel with master's degrees or doctor's degrees in the science departments is closely related to basic and initiative R&D and characteristic of our nation compared to other Western nations. Under such circumstances, the Policy Outline seeks to train and secure talent such as young researchers while taking heed of the demands of rapidly progressing fields.

3) Strengthening S&T Promotion Base

Along with the rapid advancement in S&T, it is becoming necessary to secure an overall supply of diversified research material such as standard substances and genetic resources, etc., due to the completion of the distribution system or the data base for S&T information.

However, there is still little accumulation data compared to the types of information involved, even in notable fields, such as in fact data including physical property data and industrial data.

Among the 1,845 data bases publicly available by nations of the world, only 18 of them were developed in Japan.

Consequently, the Policy Outline aims at not only the production and distribution of S&T information but also for the development, preservation, and supply functions of genetic resources, materials, and equipment which are difficult to handle by private enterprises.

4) Promotion of International Cooperation and Exchange of S&T

Recognizing the importance of Japan's active contribution to the world society in S&T, the Policy Outline raises an internationally open R&D system by appointing and receiving foreign researchers in universities and national research institutions. It also proposes measures such as promotion of diversified, international joint research and exchange of researchers and information.

5) Gaining Better Understanding and Cooperation by the Nation

Today's S&T has penetrated and caused great influence in every aspect of the nation's living. Thus, it is important for the people to have even a greater understanding and familiarity with S&T in daily affairs and create an environment which can effectively use it. The Policy Outline proposes to take proper measures to gain better understanding and cooperation by the nation which may lead to greater interests by the youth of the next generation towards S&T.

III. Promotion of Priority R&D Fields

In order to promote highly creative S&T, it is necessary to establish a system which emphasizes basic and initiative S&T while also taking the above-mentioned measures commonly applicable to the respective fields. In the Policy Outline, S&T fields to be promoted by the nation are categorized into: 1) basic and initiative S&T which can expect new developments; 2) S&T to activate the economy; and 3) S&T for the qualitative advancement of society and living standards. Basic and initiative R&D of not only item 1) but also 2) and 3) will be promoted.

The Policy Outline also proposes to set up a basic R&D plan for each field to be promoted on a priority basis by the Prime Minister. There are presently three plans of this sort set up by the Prime Minister after deliberations by

the Scientific and Technical Council, for energy, life science and disaster prevention. Other basic R&D plans will follow in due order mainly in the basic and initiative R&D fields.

S&T White Paper Outline

Tokyo PUROMETEUSU in Japanese May 86 pp 15-20

[Article by Research Division, Planning Bureau, Science and Technology Agency]

[Text] The S&T White Paper for FY 1985 was reported in the cabinet meeting on 6 December 1985. Its objective and outline were introduced as follows:

1. Objective of This White Paper

As technological innovations have rapidly advanced industries and societies worldwide, S&T has also played an important role in our nation as the motivating power in advancing the nation as an economic society. This role of S&T is expected to become even more important as Japan must cope with various issues involving the transition to an information society and advanced aged society or increased trade friction while expanding itself within an international cooperation system.

S&T is attracting greater attention from the nation than ever before, as seen in the success of the International S&T Exposition held in Tsukuba Science City. This exposition held under the theme, "Harmony Between S&T and Man, His Residence and Environment" attracted over 20 million attendants from the nation and abroad. Various movements leading to the shift from R&D based on revision and development of existing techniques to R&D stressing creativity are also becoming active.

Under these circumstances, this white paper elucidates the newly developing R&D activities and their problems, mainly for the private sector and further issues on S&T policies for our nation to make even greater progress, in Part 1. In Parts 2 and 3, trends of S&T activities and governmental measures of FY 1984 are mainly discussed.

2. Outline of Part 1

New Developments in R&D and Age of Tieups

① Advancing R&D Ability

(a) S&T Standards and R&D Potential of Our Nation

The S&T of our nation has greatly advanced due to the import and absorption of the latest Western high-technology and strengthened R&D activities during 1955-1965. After 1965, the technical development in environmental pollution prevention technology, resource preservation, and energy saving technology, mechatronics, etc., have made marked progress.

The S&T standards which Japan has reached today lay between the United States and Western Europe in terms of R&D potential for the future. In detail, such standards are high in fields with greater private incentive and user demands, as three-fourths of our nation's R&D spending is borne by the private sector. Meanwhile, these standards are relatively low in fields which require large-scale technical systems or basic software or which have comparatively low demands by private businessmen.

It is thus necessary to grasp such movements of the private sector to consider the course of the nation as a whole for the promotion of future S&T.

(b) Activating R&D Investment

Regarding the relationship between trends and results of R&D investment: 1) the role of technical advancement in our nation's economic progress is high; 2) the size of R&D investment is closely related to the technical standards when categorized by industries; and 3) a relationship is seen between investment in basic research and the amount of high-tech related theses when categorized into basic, application, and development fields. The result in S&T is "those who work hard are rewarded." Thus, the private sector faces greater incentives for R&D investment.

Facing a hostile environment, both internationally and domestically, Japanese enterprises are starting to stress R&D. The majority of these enterprises are regarding R&D as a priority item of management strategy. Enterprises with original strategic policies, determining R&D expenses on a long-term perspective are also increasing. As recent R&D expenses of the nation are increasing at a pace that will surpass the growth of the gross national product considerably, it shows a development indifferent to the effects of business fluctuation.

The ratio of enterprisal R&D expenses to sales, shown in Figure 1 is classified into Group A for enterprises with over 4 percent, Group B with a ratio of 1.8 percent to 4 percent and Group C with a ratio less than 1.8 percent. Group A mainly consists of advanced technology related industries which include communications, electronics, electric measuring instruments, and medical products industries while Group C includes technically matured industries to some extent such as iron and steel industries and textile industries. Group A has the largest number of researchers per 10,000 personnel followed by Group B and C in written order. Japanese enterprises which are closely related to high-tech goods tend to depend on researchers when conducting R&D.

Japan's R&D capabilities have markedly advanced after entering the technological innovation period the latter part of the 20th century. While Japan has reached an internationally competent level to conduct original R&D full scale, following the Western nations with R&D manpower and the amount of intellectual stock at an international level, it is still behind in respect to the peripheral conditions leading to qualitative and original aspects in R&D.

Our nation is surpassed only by the United States and the Soviet Union in total number of research personnel, many of whom are in industries. Moreover,

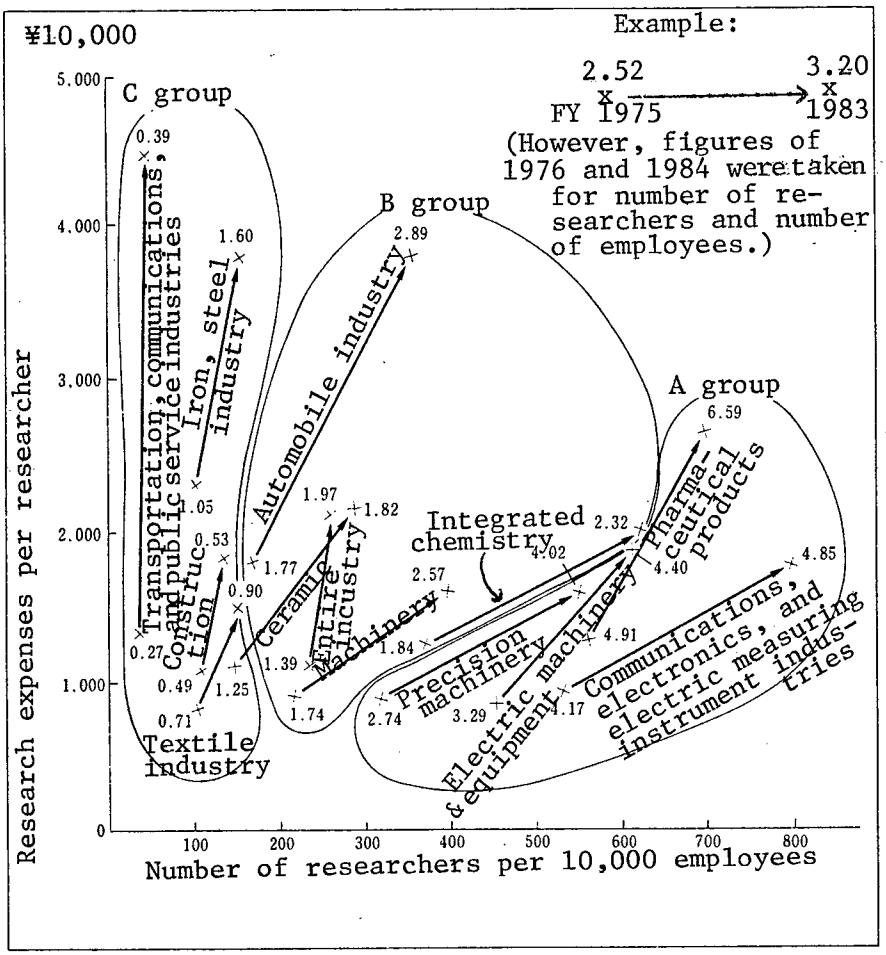


Figure 1. Analysis of Ratio of Research Expenses to Sales Output

such personnel tend to gather in fields with active businesses which further increases the vigor of the field.

While as a whole, the enterprises' manpower is further expanding, the lack of personnel in high-tech fields such as life science, information, and electronics and basic science fields is serious. Consequently, further improvement of personnel to these fields is demanded.

As we try to count the intellectual stock of S&T as an index obtained by combining cumulated R&D expenses and lost value in the information acquired by the R&D, considerable progress is seen mainly in the high-tech related fields recently. Although this amounts to merely one-fifth of the U.S. figures in total, our growth rate exceeds the U.S. rate. Thus, the difference between the United States and Japan has been diminishing in terms of intellectual stock (Figure 2).

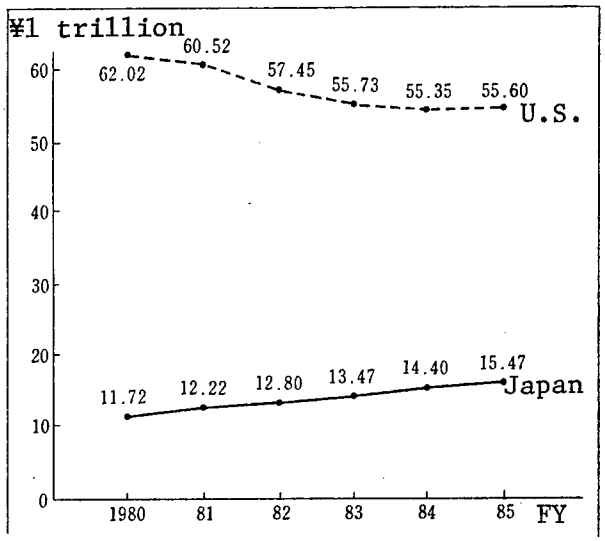


Figure 2. Comparison of Japan-U.S. Intellectual Stock in S&T

Note: The intellectual stock of both the United States and Japan concerns the whole industry.

② R&D Activities in Search of New Technology

(a) Structural Change in S&T

The nation's major interest in S&T has shifted from environmental pollution to safety problems to energy problems, in that order. At present, issues such as information S&T and life science are attracting attention. Meanwhile, the nation's consciousness has also shifted from materialistically to spiritually which is reflected in the trends of S&T such as "advancement of minuteness," "increasing emphasis on software," and "deeper relations with man." While marked progress on the first two trends is seen, the problem of S&T's deeper relations with man is a great issue for the future.

(b) R&D Activities Showing New Development

The business strategies of enterprises in respect to techniques and products and the market, are making a transition from expansion of the existing market due to application or acquiring high-value added to the presently owned technology and products to advancement into new markets by exploiting new techniques and products.

In order to develop remarkable new technology, completion of basic research is a requisite in the case of enterprises. Looking at the enterprises' engagement with basic research from the consciousness of the concerned researchers, there is an increased emphasis on creative research, especially research with non-continuous objects. Recently, basic research expenses of enterprises is also increasing at a rate exceeding the total research expenses. Thus, enterprises are emphasizing basic research, both in consciousness and actual investment.

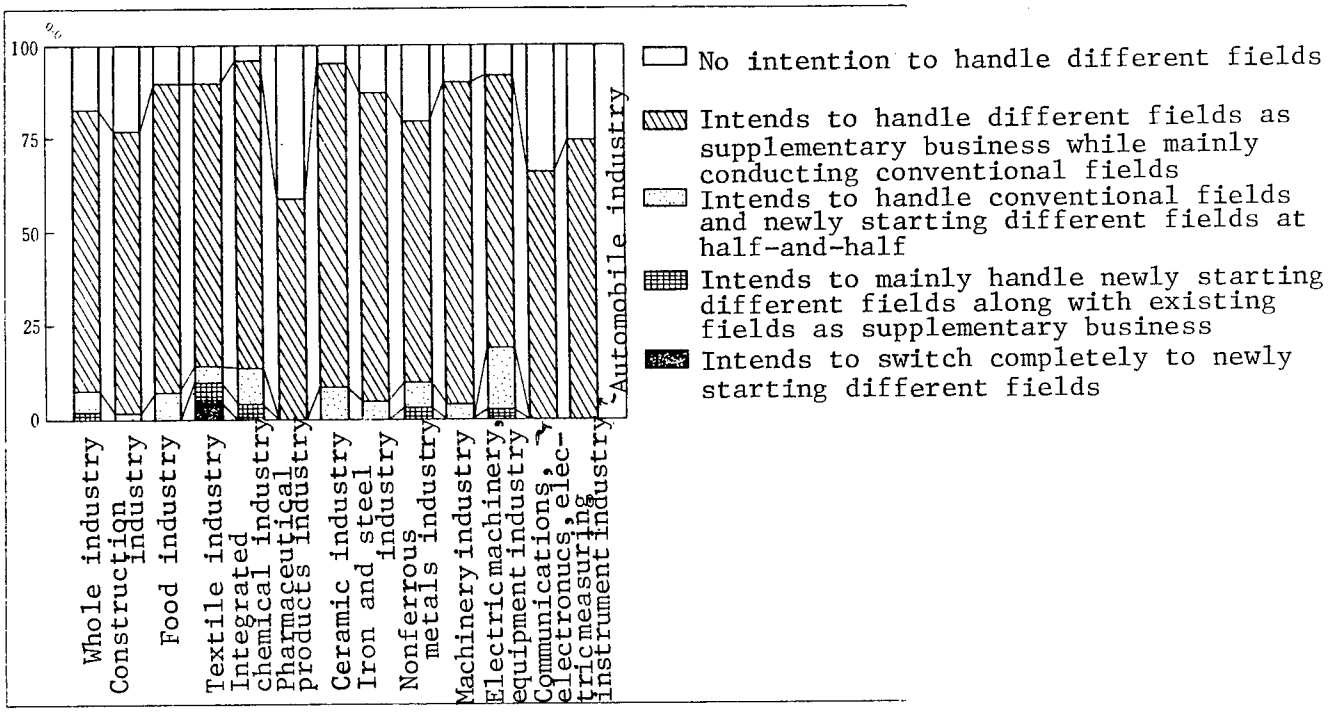


Figure 3. Intentions of Enterprises for Advancement Into Different Fields

Enterprise advancement into different fields is also activating for future survival and business scale expansion. Enterprises considering this advancement are said to be approximately 75 percent (Figure 3).

Information processing, life science, and new materials are typical high-tech fields which are expected to yield numerous new technologies in the 1990s and are watched by many enterprises for advancement. While the research share of these three fields compared to present sales is extremely low, research expenses and talent are growing in ratio.

(c) Cooperative Relations Expanding Towards New Development

There is less flow of research expenses between industries, universities, and governmental organs in Japan compared to the major Western nations. However, as the sphere of R&D with which each organ cannot cope alone is expanding, in the midst of movements to strengthen basic R&D fields and to advance into different fields other than an enterprise's specializing field, this flow between the sectors is expanding (Figure 4). The flow of enterprise research expenses abroad is also growing considerably, more so than the flow to other sectors within the nation, although very little is received from overseas nations. While the Western nations have an excess of imports over exports in research expenses, our nation's outgoing research expenses are markedly higher than the importing research expenses.

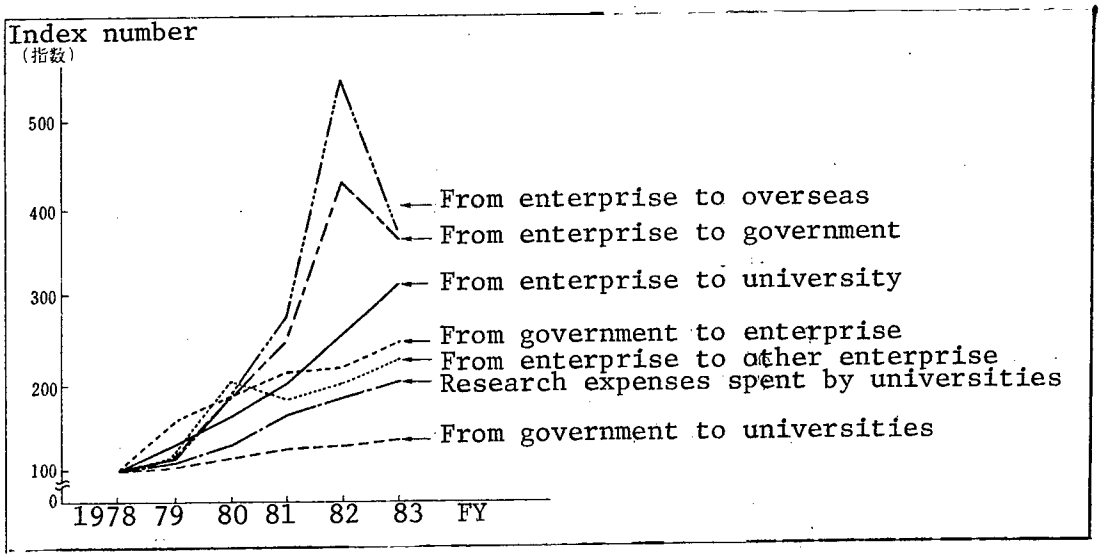


Figure 4. Increase of Research Expenses Flow

Note: The index number is calculated with figures of FY 1978 as 100.

The fluidity of research personnel is less than that of research expenses but is expanding. The amount of transfers are higher in enterprises, universities, and national research institutions, in this order, according to the expanding conditions of each sector's research activities. However, enterprises place greater weight on newly graduated students while national research institutes employ more experienced personnel. In case of expanding the existing research fields, research personnel are supplemented by transfers within the organ or employment of new graduates. As for new research fields, national research institutes tend to reorganize as the number of regular staff is restrained while many enterprises employ experienced personnel from outside the company.

Approximately 70 percent of the enterprises expect to stress independent research and the ratio of enterprises which intend to emphasize tieups with other organs is also increasing. As a whole, enterprises are expanding cooperative relations including those which plan to cooperate with other organs in some form, if not with priority.

Cooperation with overseas organs is also steadily increasing along with increased joint research, consignment research, contribution to universities, etc., since 1975. Tieups between enterprises and overseas organs differ in character by their form. In the case of joint research, the other party is another enterprise and mainly application and development research is handled to cope with market demands. The partner of consignment research is from private research organs, enterprises or universities engaged in basic fields.

(d) Measures of Nations Showing Greater Similarities

Looking at the share of research expenses by industries of the world nations, electricity, electronics, chemistry, medicine, etc., rank at the top of the major nations except for the United States, which has aircraft at the top, in respect to research expenses. Thus, most nations can be said to have a fairly similar industrial structure.

Research fields promoted by the governments are similar in placing priorities especially in high-tech fields, although the major European nations are stressing general scientific research while the United States is investing overwhelmingly more for national defense, space, medicine, and energy projects. Mutual influence between the nations is also expanding by adopting each other's advantages in their projects. Such a tendency is also seen in the tax system of the nations for S&T promotion. Cooperation between different fields which has become especially necessary recently and measures to promote tieups between industries, universities, and governmental institutions are also strengthened by each nation.

③ Issues for Japan's Future Progress

(a) Strengthening Innovative Creativity by Nation as a Whole

With the creation of original S&T becoming more important in our nation, a structural revision of R&D is becoming necessary.

Japan's investment in basic research per capita which becomes the basis of such activities is relatively smaller than Western nations. Basic research expenses by governmental research institutions are especially small and there are also few organs to join S&T. Although measures are taken to cover the weak spots of our nation's S&T, including the exploratory research for Advanced Technologies System, a revised research operation to strengthen basic research in national institutions and generate innovative basic research is a requisite.

(b) Advancement of Motive Power for Innovative Basic Research

The balance of investment to basic, application and development research in our nation has a similar structure to that of the United States. However, our outcome is one step behind the United States which has activated wider-ranging R&D activities and has yielded many new technologies. As our nation has attached importance to the practical application of technologies, they have been greatly affected by the trends of the users. Large-scale developments, such as for the bullet train which has helped advance our nation's S&T, have also decreased in number. Consequently, setting up projects which may draw out new S&T for basic research and innovative new technologies and not only practical application and completion of a promotion system are required.

(c) Expansion of Basic Research and Revised Operation of National Research Institutions, Etc.

While the role of enterprises in our nation's R&D activities is large, there is a limit in large-scale technologies which can be handled by larger enterprises and also in basic research due to the object of its activities which may not suit the enterprises' intentions. Thus, there are also many areas where the public sector can play a great role. Much of the research which private enterprises expect national institutions to handle is basic research, especially in the high-tech related fields. Thus, it is necessary to strengthen measures to cope with these demands. In order to revise research operations, completing conditions for young and capable researchers such as by forming basic research groups consisting mainly of young researchers, as well as training and securing experienced research leaders is required. Setting a target to promote research which is supported by concentrated efforts to accomplish a definite objective and revising research operations are also demanded in basic research.

(d) Completion of Environment for Tieups

While there is an increased demand for tieups with national research institutes in the form of technical guidance, technical consultation, consignment research or joint research, they have not been able to fully meet these demands due to personnel or specialty restrictions. Consequently, it has become important to complete a cooperation network between universities and enterprises and a system to meet the expanding demands for joint research and also to revise its operation accordingly. While various systems are provided to promote industry-university-government tieups, these tieups are still in the beginning stages as a whole. Thus, full-scale promotion is demanded.

3. Conclusion

With greater influences of S&T in the advancement of our economic society and in the nation's living standards and social flow from quantity to quality, competition between enterprises is becoming even more severe. Thus, R&D investment for future returns by enterprises is a great motivating factor in the progress of our nation's R&D activities.

Accordingly, the scale of Japan's investment, personnel, and S&T outcome has become fairly large, although there are still various problems as a whole. A new development towards qualitative advancement is required.

Under these circumstances, our nation's interest in S&T is shifting from quantitative sufficiency to qualitative sufficiency including humanistic and cultural properties. It is also becoming important to exploit original new technologies which can contribute to the prosperity of the international society and win international confidence, at the same time.

These developments can be effectively forwarded only after the formation and accumulation of S&T intellectual stock which has historical and cultural depth and quality. Completion of environmental conditions to allow researchers to bring out their originality is also a requisite.

Consequently, our nation's S&T policy requires the following measures in order to strengthen the creation of original S&T.

(1) Basic research from the public sector which is still relatively weak will be strengthened and completed in order to form high quality S&T intellectual stock, as the source of a new technological creation.

(2) Projects which may draw out new basic research S&T will be set up and a means to promote such research will be completed.

(3) Basic research will be strengthened in national research institutions which should play a considerable role in promoting the foundation of new technological developments in our nation. Its operation will be revised accordingly for researchers to display their abilities.

(4) In the midst of movements to expand the base of basic research fields, to advance into different fields and to introduce high-technology into local districts, environmental conditions to promote technical guidance, research cooperation, etc., by the public sector which is said to have many restrictions will be completed in order to cope with the increased demand for tieups.

Promoting Original R&D

Tokyo PUROMETEUSU in Japanese May 86 pp 21-24

[Article by Seiichi Watanabe, Planning Section, Planning Bureau of Science and Technology Agency]

[Text] Owing to the rapid progress of our nation's S&T standards, our industrial technology is highly acknowledged in the world market today. However, as the fundamental basic technology still largely depends on imports from overseas, such a constitution must be revised in order to produce original S&T for the stable economic advancement of the nation and contribution to the world economy.

The Science and Technology Agency has consigned an investigation on the "Conditions for Promotion of Original R&D" to the Nomura Research Institute of Technology and Economics, as part of the basic survey of S&T policy supported by S&T Promotion Coordination Expenses.

In this investigation, marked R&D cases were analyzed and the conditions of the present R&D promotion system were also surveyed while considering the conditions required to promote original R&D in the future. A brief summary of the outcome is reported as follows:

1. "Originality" Demanded in Our Nation

In this investigation, types of originality were systematized into three axes, namely, academic impact, R&D process, and economic impact, as shown in Figure 1.

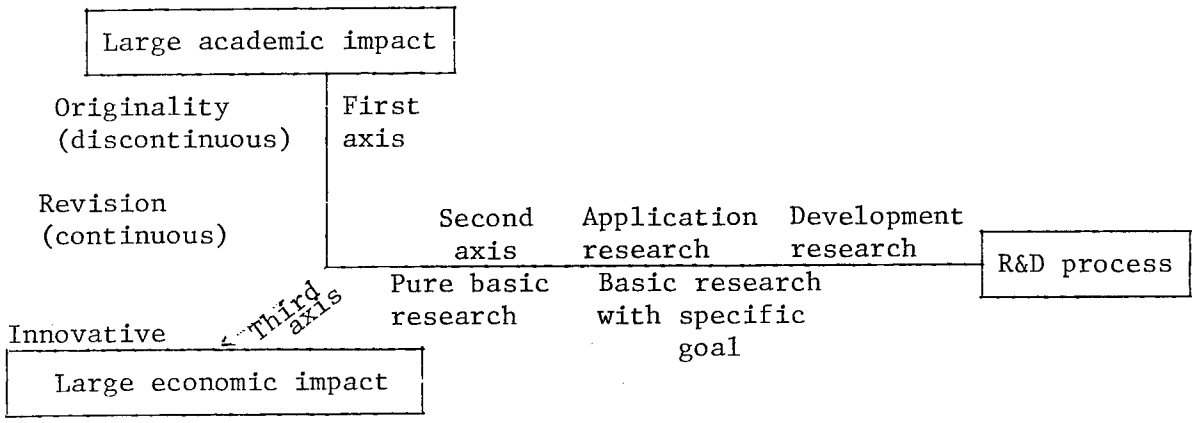
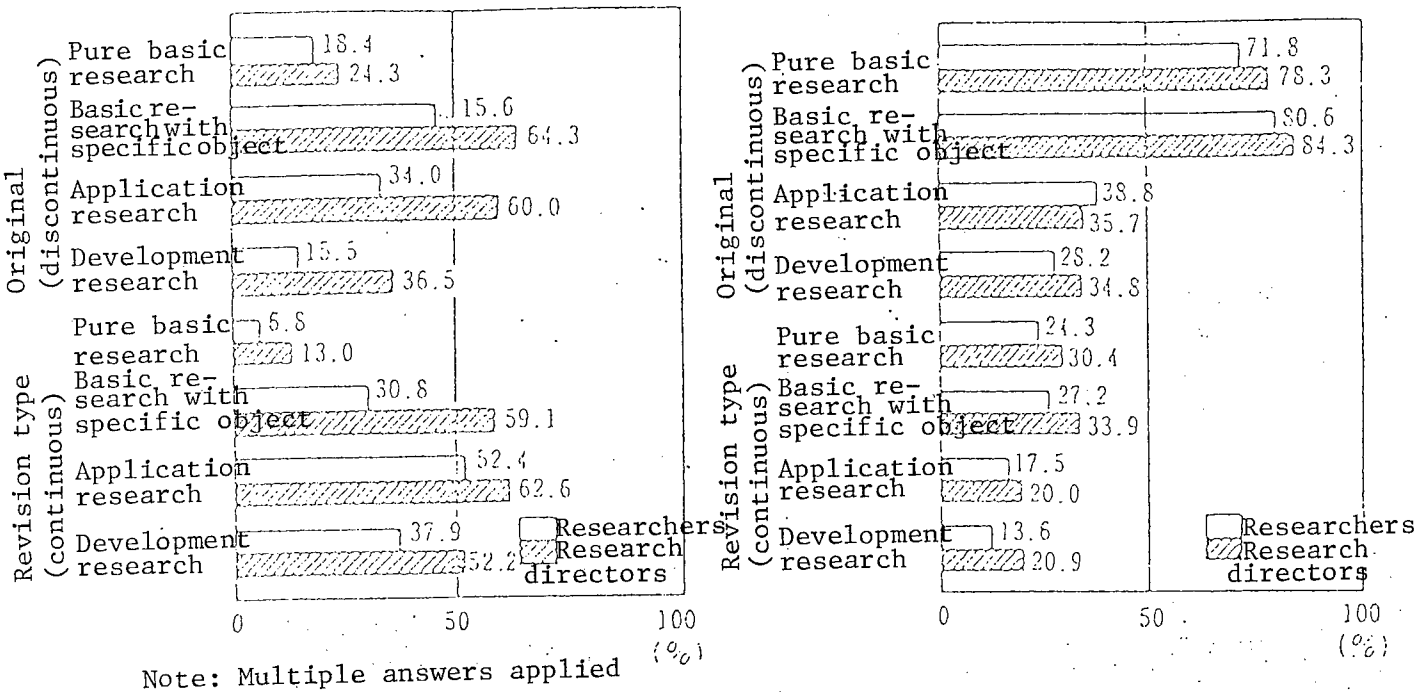


Figure 1. Types of Originality

Our nation's R&D has been forwarded mainly in the revision type application and development research in this categorization. This was endorsed after results of investigating five typical R&D cases and studying at which step and what type of original research was required in these cases. Japan's contribution was found in application and development research but rarely in the basic research fields.

Figure 2 is the outcome of a questionnaire sent to univerisites, national research institutions and representative research organs of private enterprises in our nation. They were asked what type of R&D they are presently engaged in and what type of R&D they consider important for our nation.



Note: Multiple answers applied

Figure 2. Existing R&D in Japan (Left) and Demanded R&D (Right)

According to this survey, resarch organs which are presently conducting original R&D amounts to about the same number of organs which are forwarding revision type R&D.

However, the type of R&D which they consider to be important in the future was overwhemlingly centered on original basic research for pure basics. This indicates there is a considerable lack of original basic research conducted in the nation.

As Japan's social economic environment has greatly changed in the postwar 40 years or so, our nation's R&D must make a shift from revision type application and development research to original basic research. Three reasons can be raised for this phenomenon: 1) difficulty of technological import;
2) advancement of our nation's position in the world economic society; and
3) expanded bases for our nation's S&T.

2. Background Factors of Past Original R&D

Table 1 analyzes the background factors of 10 original R&D cases by categorizing such factors into individual factor, organization factor, and social culture factor. Based on this case study, general conditions to promote original R&D were reported, as follows:

(1) Individual Factor

Curiosity and a critical mind which are largely affected by one's childhood environment and education are important points.

In considering original R&D, the buds of curiosity must not be picked away by placing too much emphasis on cramming knowledge.

Fostering tenacity is also considered to be deeply involved in this educational issue. While contemplating or experimenting until one is fully convinced of some doubt in the existing education system is an attitude which we are apt to forget, ascertaining the true nature of matters and grasping how to approach them is required in the education, of all things.

(2) Organization Factor

Forming a system or grounds which will allow young researchers with abilities to be promoted to respectable positions at an early age is most important.

In order to realize such an assignment of scientific elites, the existence of research managers with just evaluation capacity is a requisite.

It is also necessary to increase freedom within the organization. For instance, it is desirable to allow free selection of research themes, time, and term of research and usage of research expenses. Free discussion between researchers inside one's organization is also required.

Table 1. Background Factors of Original R&D Cases

Name	Individual factor	Organization factor	Social & cultural factor
Reona Ezaki	Accurate observation	Organ promoting autonomous research	
Minoru Oda	Wideranged curiosity Concentrated thinking for long period	Fortunate with teachers and friends	
Akira Sotomura	Concentrated thinking of one theme, with patience	Japan Central Research Institute recognized voluntary research Hitachi had a climate of emphasizing R&D Existence of research director who guided him Accumulation of techniques	
Junichi Nishizawa	Contact with science from early age, good environment for thinking, perseverance to trace a matter thoroughly Unyielding, hardworking spirit	Good tradition of Tohoku University for R&D	
Mitsunobu Okamoto	Acquisition of sense of success at youth Extensive curiosity and perseverance	Free research system Just assessment by research director	
Kenichi Fukui	Perseverance to pursue thoroughly	Backup by teacher Fortunate with research operators	Bonus received at youth
Mitsuaki Koyama	Concentrated research with bright passion Became independent when still young and researched freely	Good tradition of Tokyo Industrial University for R&D	
Juzo Udaka	Coexistence of perseverance and quick mental switchover	Free and complete research environment Proper advice of teachers and parents	
Yoshio Okada	Acceptance of wonders readily Repeated experiments with perseverance	Free research organ with active gatherings Ample research funds and complete experiment facilities	

[continued]

[Continuation of Table 1]

Name	Individual factor	Organization factor	Social & cultural factor
Yasukazu Nagano	Pursuit of one theme by steady and hard work Valuing a sense of wondering Modest research attitude	Lenient research organization and tradition to meddle in research Sufficient staff and facilities	

(3) Social and Cultural Factor

The advancement of the social status of researchers becomes an important factor. This can be realized by attaching priority to science as a social trend by systematic changes, such as improving the incentive system.

2. Present Conditions and Problems of Original R&D Promotion System

In order to bring about original R&D which is demanded in our nation, problems in the R&D system of universities, national research institutes, and private enterprises, must be considered. Thus, factors which were hindering original R&D in these organizations were studied in this survey, through questionnaires from leading research institutions. The results are as follows:

(1) University

Obstructive factors which are hindering original R&D in universities at an individual level are "difficulty in raising subjective researchers," "lack of individual researchers," and "few researchers with abilities to debate" according to 60 percent of the researchers and research managers answering the questionnaire (multiple answers).

Regarding organization factors the majority of the respondents raised, "few unique research themes," "rigid professorial chair," "few reshufflings and interchanges of research personnel," "lack of research expenses," "little freedom in usage of research expenses," "inability of researchers to fully devote themselves to research," "weak system to support research," and "lack of research facilities and equipment."

In the social and cultural field, approximately 40 percent of the respondents gave "lack of competitiveness" and "low social evaluation of research" as obstructing factors.

Consequently, the major obstructive factors of original R&D in private enterprises can be said to emerge from lack of personnel changes, "few reshuffling and interchanges of researchers," monetary shortage indicated in "lack of research expenses," and "researchers' inability to fully devote themselves to research" which is caused by the "weak support system."

(2) National Research Institutions

As an individual obstructive factor in national research institutions, "increasing number of advanced age researchers" is a major problem. The majority of the respondents also raised "few researchers with the ability to display leadership" as a problem.

In respect to the organization, "difficulty in autonomous research is from a long-term perspective," "rigidity of organization," "few reshufflings and interchanges of researchers," "little freedom in usage of research expenses," and "few research managers who emphasize originality" were problems raised by the majority.

As social and cultural factors, "lack of competitive spirit" and "low social evaluation of researchers" were raised by 60 percent of the respondents.

The major obstructive factors in R&D by national research institutes are an increase in older researchers, difficulty in conducting autonomous research from a long-term perspective and lack of research managers who emphasize originality.

(3) Private Enterprises

Factors raised by the majority of respondents of things that obstruct original R&D in private enterprises were, "few individual researchers," "inability to return to the fundamentals in research," and "lack of research managers who emphasize originality."

Based on the mentioned questionnaire and interviews of research managers, the issues of original R&D in universities, national institutes, and private enterprises were listed in Table 2.

4. Conditions To Promote Creative R&D

Detailed conditions for the promotion of original R&D are introduced in the following items which are the results of this investigation.

(1) Home Background To Bear Originality

The seeds of originality are considered to be nurtured by curiosity, gentleness towards nature, and a love to debate. In order to nurture such seeds: 1) a house with an atmosphere to study; 2) a mother who does not force a child to study; 3) a home with intellectual stimulation and frequent family gatherings for conversation; and 4) a lifestyle communing with nature are required.

(2) Education System Which Does Not Deprive the Seeds of Originality

The present education system is effective in raising cooperative students with high standards on the average, but is possibly depriving originality from the children. Consequently, 1) education emphasizing experiments, observation,

Table 2. Issues of Original R&D Systems

Factors	Original R&D Promotion Conditions	Universities	National research organs	Private enterprises
Individual factor				
(Age)	Young	△	x	△
(Ability)	Individual	x	x	x
	Subjective	x	x	x
Organization factor				
(Operation)	Autonomous research allowed	△	x	x
	Long-term research allowed	△	x	x
(Organization)	Flexible organization	x	x	o
(Gatherings)	Various matching of personnel	x	x	△
	Active discussions	△	△	△
(Assessment)	Assessment of business results on long-term perspective	x	△	△
(Treatment)	Changed according to research results	x	x	△
(Research expenses)	Sufficient research expenses	x	x	△
	Research expenses used freely for a long period	x	x	△
(Research director)	Emphasizes originality	△	x	x
	Responsibility and power are fully transferred to research director	△	△	o
(Research environment)	Full support of research assistants and secretaries	x	x	o
	Up-to-date facilities available	x	△	△
	Complete analytic service of experimental information and information retrieval service	△	x	△
Social and cultural factors				
(Competitiveness)	Research organ with active competition	△	x	△
(Salary)	First-class salary standards	△	△	o
(Research elite)	Climate approving research elites	△	△	△
(Bonus)	High bonus	△	△	△

o Little problem
△ Moderate problem
x Significant problem

and discussion; 2) class arrangement by subjects grouped by ability; and 3) revision of the education system such as introduction of skipped classes.

(3) Fostering Research Elites

As the peak of original R&D ability is considered to come at about 30 years of age, research elites who can take up autonomous research around this age and freely apply personnel and monetary resources to some extent, must be fostered. In national research institutes for example, research teams may be arranged with young researchers as project leaders.

(4) Research Assessment With Priority on Originality

If research managers place importance on originality, organizations must naturally move towards yielding originality. Consequently, it is necessary to establish research assessment with priorities on originality. For instance, researchers of universities and national research institutes must also be fully evaluated and their research performances must be treated accordingly.

(5) Flexible Organization

An environment which will bring about original ideas is required. In other words, formation of project teams by researchers of different fields and backgrounds and an environment of active discussion must be provided. Thus, personnel reshuffling, meetings by researchers, and promotion of joint research between industries, universities, and governmental organs are required.

(6) Completion of Incentive System

Japan is said to have very few incentive systems compared to the United States. Thus, establishment of a private foundation to collect funds for promotion of S&T and provide an incentive system is required.

Private Sector Research Strategy

Tokyo PUROMETEUSU in Japanese May 86 pp 25-33

[Text] Japan's S&T is in full operation today, starting with industrial technologies such as electronics, materials, and biotechnology which have achieved especially marked progress. However, it is also true that our nation's attitude towards product development has been criticized by other nations, causing trade friction. Thus, managers of eight private companies were asked about their engagement in basic research.

Establishment of New Research Center in Keihanna Science City

Kyocera has been engaged in basic research related to electronic equipment, optical equipment, and fine ceramics which caused a material revolution. Material related basic research starting with fine ceramics is conducted at the General Research Center in Kokubun City of Kagoshima Prefecture. Plans to build a new research center in Keihanna Science City have been forwarded

along with a project to conduct mainly ceramics-related basic research at this center. The General Research Center is operated by two groups, namely, the material development group and the project development group. While the applied material widely varies, basic research is conducted to raise specialists in the respective fields. The project research group handles much consignment research from businesses. In 1986, development of AGT (advanced gas turbine) will be researched. Among the approximately 130 staff members of the General Research Center, the ratio of those engaged in basic research to project research is about six to four.

Difficult Handling of Pure Basic Research

In basic research, there is "pure" basic research such as that conducted by universities and national research institutes and basic research aimed at a certain objective. Pure basic research is difficult for enterprises to handle due to restrictions in the number of personnel and the wideranging themes concerned. Thus, basic research with a definite objective is more often handled. For instance, as the technological abilities of materials have a great influence in our future, a research center must raise and keep specialists of the respective material or process such as that of alumina or casting technology. This in fact, is basic research. Japan's ceramics R&D is still behind the United States in the basic research field.

Research Project With Strong Leadership

In respect to joint research between industries, universities, and governmental organs, I have an impression that in the United States, leadership is fully displayed in projects and more effectively operated than in the Japanese systems. Our nation's original R&D promotion system should be considered in this sense. In Japan, personnel from many enterprises and different fields generally gather in such joint research, often resulting in over florid composition. While leveling up as a whole and mutual stimulation are naturally required, a project may be more effective with definite leadership and systematization.

Kyocera keeps the so-called Kyocera professors at the Massachusetts Institute of Technology, Case Western Reserve University, and Washington University in the United States which is a practice unseen in Japan. The company is sending young personnel to American universities to receive qualifications as graduate students and is also assigning four to five researchers to domestic universities and national research institutes such as the Japan Institute of Electronics or the Osaka University each year.

On the other hand, we will heartily welcome any proposals to researchers of national research organs or university research rooms sent to Kyocera, not only for 1 or 2 years, but preferably for a longer term.

R&D conducted by NEC consists of seven units, that is, six research centers and one development headquarters called the "R&D Group," where a wide range of fields, materials, devices, equipment, systems, biotechnology, etc., are studied and developed. We have set up this research system as "R&D for Future Businesses" in which the respective groups bear their own responsibility.

A basic research center is provided in this group which focuses on totally new research fields where NEC Corp. does not possess any technology yet. It has been established from the standpoint that Japan's enterprises must also increase the ratio of pure basic research, in the midst of high-tech friction.

Closely Related New Technological Development and Regional Culture

Only 100 years has passed since Japan started its course as a modern industrial society. During thistime, every possible technology was imported from the Western nations and revised to meet the demands of the respective periods. Our present progress was never obtained, if these technologies had been developed in our own nation. We can interpret the rising call for basic research from every sector of the nation as the fact that Japan has finally acquired room for such research. Japan has also graduated from an industrial society and entered into an advanced information society. The technologies of the past were closely connected with "matters," whereas in case of an advanced information society, "man" is a very strong factor. In other words, technologies are closely related to regional culture and the nation's individual culture. For instance, the relationship between computer terminals and keyboards and the Japanese language is a good example. The resulting basic technology is a valuable technology not only in Japan but also in the Western nations. Speech recognition technology and pattern recognition technology which are considerably more advanced than in the Western nations were also achieved by the pressing problem between technology and culture and regional demands.

In case of electronics technology, Japan has surpassed the West in some areas but for the most part has only come to rank with these nations. Basic technology is also way behind.

Gatherings Between Researchers of Different Fields Demanded

With the advanced information society, we have entered a difficult age in which its advanced demands cannot be met without mutual stimulation between various fields and compounding various types of technologies. Consequently, gatherings and cooperation between different fields have become a requisite. Such activities have become quite active in Japan, in some aspects exceeding overseas nations. An outstanding idea or originality does not emerge when researchers of the same nature join together. Although individual originality played a great role in the past Western industrial society, individual concepts or ideas alone will not allow us to confront the future.

Gatherings of Researchers and Public Servant Law

A research system suitable to such an advanced information society is actually underway in Japan. However, the breakthrough must be made by an outstanding idea or originality of an individual. This becomes the impetus. Thus, personal exchange between researchers is an important issue. In Japan, there are systematic and organizational difficulties. Due to the Public Servant Law, researchers of national research institutes and national universities cannot stay in private enterprises for lengthy periods, although the opposite is possible.

In private research centers, there are numerous technical problems which can be solved by accumulating basic research. There are gems which may sparkle if cut properly. I hope some of them will be cut with the help of researchers outside the enterprises, if not all. It is thus necessary to make a system to allow these researchers to come to private research centers for a certain term. In this way, basic research can be conducted by each company for their respective businesses. Basic research by private enterprises must also be forwarded so that it can properly assess the excellent university research. There have been cases of reimportation of such research from abroad in the past, due to the lack of foresight by enterprises, although such research naturally may not have been demanded by Japanese society, at that certain period. We must be able to acquire the ability to perceive enough from few guidances rather than learning everything from university professors. Without this, cooperation between industries and universities cannot be achieved in the true sense.

Progress Based on Amino Acid Fermentation

Our company was originally a research center at its foundation. Even through its history, it has grown upon the outcome of basic research. Amino acid fermentation which is one of the company's foundations is also in a sense, basic research. Not only were we the first to make amino acids directly from sugar with microorganisms but we have also succeeded in making glutamic acid or lysine by technically controlling the power of microorganisms. In the pharmaceutical products field, we have developed streptomycin jointly with Melk of the United States, due to national demands at the time and make social contributions as an enterprise. Mitomycin C, an antibiotic was discovered and industrialized with the cooperation of Dr So of Kitazato Research Institute. These are in a sense basic research in search of antibiotics. In the biotechnology field, we have been quick to handle new biotechnologies such as gene recombination, cell fusion and mass cell culture. While it depends on where the border of basic research is placed, we are continuing our "basic" research to become the foundation of new fields.

New Light at Biotechnology Research Center

In spite of the flashy talk about biotechnology, it is essentially a "technology." While it has a scientific base, it is still a technology, at the present stage. The present issue is what to apply biotechnology for, that is, what to produce using biotechnology.

Our company established the Kato Bioscience Research Center in 1983, partly to execute basic research apart from research for application or practical usage. Bioscience research will be strengthened in this research center as a thinktank with international perspective. It expects to cast new light on bioscience in 10 or 15 years time, as a field deeply involved in the latest studies. The greatest theme to be handled will be "aging." An external symposium which was held last November on this theme was very successful as it apparently was an interesting theme.

Further Advancement of Industry-University-Government Joint Research

As joint research, one company is participating in a new company to research protein engineering. This company which will be jointly established by five firms is expected to acquire approval for investment by the Basic Technology Promotion Center of the Ministry of International Trade and Industry and the Ministry of Posts and Telecommunications.

We believe joint research of basic fields by industries, universities, and governmental organs has high prospects and we hope it will expand ideally. This will require sufficient guidance, policy-wise. The adjustment between the five ministries, however, does not necessarily seem to be working well at present. The research of protein engineering for example, should be allotted a longer term than just 2-3 years and have a guaranteed budget. If I may, I wish that the idea of science which does not yield profits is understood. If only the government was willing to allot some of its budget to be freely used for science....

"Stock" and "Flow" of Technology

The term "expansion of intellectual stock" appears in the S&T White Paper of FY 1985. While the technological trade balance has improved considerably there is still an import surplus. Japan's technology can be said to be in the "flow" stage, lacking in "stock" like its economy.

Although our country is called a technological or economic giant, we are still basically very weak. It is merely 100 years since Japan started to industrialize and in the world of chemistry, enterprises of the Western nations have imposing histories compared to Japanese enterprises. The chemical industries of Germany especially have over a 1,000-year history based on its own S&T.

Except for the prewar alkali industry, the chemical industry of our nation should be considered to have started along with the sudden growth of the petrochemical industry. Most of its basic technology was imported from the Western nations. As a result of revising these technologies and accumulating related application technology, Japan has surpassed these nations in manufacturing technology. Japan also does not yield to the West cost-wise. Its pollution prevention technology for example, must rank No 1 in the world.

Field To Be Emphasized With Limited Resources

As the technological export of the chemical industry has gradually increased, the technological trade balance has come on the surplus side. This is also due to the difficulty in purchasing techniques from abroad recently. Although the necessity of basic research is called for in order to yield new product technology for the future, basic research requires time and accompanying risks where there are no guarantees of success. Consequently, the enterprise must have considerable strength. Our company has established the Life Science Research Center and Plant Engineering Research Center to conduct basic research while also executing investigative research in the General

Research Center. Which field should be emphasized to what degree within a limited framework of resources is a great issue for the future.

Policy of Research System

While there are various research organs and systems under the Science and Technology Agency and the Ministry of International Trade and Industry [MITI] in the nation which have borne respective fruits, most of them are single projects. In order to make these systems available to the chemical industry, they must become collective and adjustable.

Basic research is considered to consist of three fields, namely: 1) fundamental research; 2) basic research; and 3) explorative research. The first includes foundation type research and the second consists of analytic research which elucidates various phenomenon by tracing their base. The third contains basic research with a specific object which is important for enterprises in order to yield new products. As these three types of basic research are correlated and interdependent, each research institute must recognize its allotted role and cooperate with other organs.

Although it is desirable that research forwarded by national research institutes and research by enterprises are mutually supplementary, this is not necessarily the case in reality. We, therefore, wish that an administrative mechanism is made for joint research in which both parties assign each other's roles.

Our company has been participating in the National R&D Programs and the Research and Development Project of Basic Technologies for Future Industries of MITI and expects to establish a new company of protein engineering under the guidance of the Basic Technology Research Promotion Center. We are also joining the Ogata Project under the Creative S&T Promotion System and also intend to join the Kuroda Project.

While joint research by enterprises and governmental research institutes must be promoted, there also are difficult problems such as distribution of research results which must be considered in the future.

How To Increase Research Stock Outcome

The results of basic research cannot be directly applied for practical usage. In order to turn them into products, enterprises must conduct large-scale development and application research.

As increased stock of basic research is a requisite in advancing our nation's technological standards today, we want to take measures in this field.

Unlike the United States, joint research with national universities is obstructed in Japan by the Public Servants Law. Some measures to improve this situation are demanded.

From Western-Oriented Development to Original, Independent Development

When considering basic research in the history of Japan's enterprises, high priority was always given to catching up with the advanced Western nations. The intention of the whole nation was directed to catching up with the West rather than acquiring originality as Japanese. This trend of the nation as a whole was seen from the education stage. Technological dependence on the West and Western-oriented technologies was no mistake.

However, this is no longer the case. We can no longer depend on the Western nations for technology. Movements to acquire original technology have also become active. This is also true in the case of enterprises. Unless an enterprise spares a part of its presently conducted research for application and practical usage of basic research, even its existence may be threatened.

Leveling Up Technology

There are two objects for basic research by enterprises. One is to create the seeds of new original technologies and the other is to bring the level of technology itself up. These activities cannot be neglected when we consider conditions 10 to 15 years ahead. Enterprises should not only forward their own research, but also conduct joint research to keep step with the basic research trends of governmental and academic circles.

Establishment of Basic Research Center

After sending "Ajinomoto" into the world 77 years ago, our company has been engaged in the multipolarization of food, medical product, and chemical product fields. We expect to further complete basic research by starting a basic research center within the year. This research center aims at producing the seeds of technology 5 to 10 years later and increase the level of technology.

It is extremely important to promote joint research between enterprises, governmental organs, and universities. In doing so, it is necessary to treat the researchers well and to make an environment which will allow each individual to fully display his abilities and express free ideas. Even if researchers apply or participate in the various systems directed by governmental organs, the ideas of individual researchers are apt to be obstructed due to strict regulations and procedures characteristic of public offices. As industries and academic institutions are in the position of conducting actual research, we expect the government to efficiently guide these two parties.

Tax Reduction and Exemption Measures for Basic Research

In promoting basic research, another issue is the tax problem. A large sum of money is required in basic research, tax reduction, and exemption measures according to research sections. I have keenly felt the necessity of such measures when calling international researchers to academic meetings, for example. I also ask for these measures to promote international exchange of researchers.

Attitude Not To "Imitate"

Japan's S&T has advanced by importing most of its basic research from the Western nations. However, with the sharply rising trade friction today, Japan is faced with criticism from the West for its lack of originality. The importance of basic research is thus advocated, although the nation is, in fact, not fully ready under the existing circumstances. Even if the required organization and funds were promptly prepared, it will take a long time.

I believe that in promoting basic research, it is important not to "imitate," not to run after the fashion and to do something different than what others are doing. Unless these values diffuse within the whole society, we will not be able to cope with the criticism of the Western nations. This will take much time. Research activities which can be entitled under the name, basic research, cannot be realized unless the attitudes of each researcher change. This is true of all the industrial, academic, and governmental sectors.

In respect to the research fields, biotechnology and protein engineering, which have been recently studied on a large scale, have become the fashion. I wish that research and industries unique to our nation will come out, rather than merely follow the fashion. I also hope that many researchers will forward research subjects other than what is in fashion.

Independent R&D by Our Nation

Much of the projects which the government is planning to promote with a budget are from these fashion fields. This may be the result of a consciousness that they will bear some fruit in the near future. Although I do not mean to comment on this, it is doubtful that they will eliminate Western criticism. I think it is possible for Japan to surprise the Western nations by yielding a research unique to our nation and industrializing it, if many people join under the same cognition.

Great Britain, for instance, is advanced in this respect, while it is behind in turning technology into products. This is an antinomy phenomenon. The British are always taking up something new for pleasure.

Concept of "Prospective Basic Research"

In order to truly promote basic research it is better not to expect anything in a short period of 2-3 years. Expecting an early outcome may miscarry a project. Thus, it is difficult for one company to conduct basic research. Although basic research is presently categorized into pure basic research and purposeful basic research, I wish to propose what may be called "prospective basic research." I believe the research conducted in our company falls under this category.

As pure basic research is difficult to handle by enterprises alone, it will be conducted as a joint project between industries, universities, and governmental organs. I hope systems such as the Exploratory Research for the

Advanced Technology System will be actively promoted by forming budgets for these systems.

Business achievements of our company have advanced in the past by synthetic fiber. Recently, we have developed unique products such as polyester film, carbonic fiber, and interferon, and also intend to promote R&D of high-tech fields.

Why is basic research required today? One reason is that Japan's technology has been realized in the past by importing ideas from abroad and forcefully manufacturing products using them. However, smaller businesses, rather than larger enterprises have rapidly acquired the ability to produce new products as they make quick decisions. Consequently, unless companies start research which may not succeed at all, foster original ideas, and obtain legal rights, development of new technology cannot be forwarded in the future. Such a sense of crisis indeed has brought out basic research.

Second, criticism from abroad is focused on Japan resulting in trade friction problems. In order to counter allegations that Japan is manufacturing products at low cost by importing technology which foreign nations have worked hard to develop and selling these products abroad, Japan must show that considerable funds are expended on inefficient basic research with a risk. Otherwise, Japan will not have the "qualifications" to sell high-tech products. Third, Japan has finally become capable of thinking about more than just profits and contributing to the world by stressing science as the common asset of all mankind. Japan must work to be respected overseas. I believe these three points are the direct motives.

"Free Research" and Attitude of Management

The secret of basic research is in "gathering capable people and having them research freely." However, there is nothing more difficult than this. There are numerous research centers which started out under the "free research" slogan but were compelled to change their course after a few years. Two problems exist. One of them is the exasperation by the management side for quick research results. The other is the "yearning for management" due to the "anxiety to be free" by the researchers. The second problem can be very hard to solve when working with young "examinee intellectuals" who are accustomed to being managed since they were born. Thus, "good researchers" who have set up their way to fortune should give other researchers a cultural shock and lead them. The attitude of management becomes important in this respect. The management side should stay composed and not make waves at the research center by expecting short-term results.

Research Plan of Basic Research Center

The research plan of the Basic Research Center is to conduct: 1) creative research activities based on the free ideas of individual researchers; 2) to foresee the social demands in 10 to 20 years and promote precedent research by focusing on key technology for social contributions; and 3) to aim at acquisitions of mainly wideranging software such as academic theses or basic patents.

The actual research consists of 100 percent "voluntary research" and no "consignment research" at all. Notable university professors will be invited as consultative advisors and research will be conducted in groups. Intermediate functions such as screening or assessment of research results will not be organized, although a gathering will be held once a week by researchers of different fields for interdisciplinary discussions. We expect to be in close contact with other research organs in the nation and abroad and activate research activities as an "open research center."

Exploratory Research for Advanced Technology Under Spotlight

The Advanced Technology System is a very interesting system. The system developed by Mr Ookawa, formerly of the Institute of Physical and Chemical Research, was one of its models. The system is based on a method which allots budgets to the chief researchers and gives them full power to act on their behalf. We are interested in the system in this respect.

The number of Nobel Prize winners is often referred to when talking of Japan's S&T. I, however, believe that Japan's potential has risen considerably. Japan will be able to expect Nobel Prizes not as exceptional cases but in terms of probability, on the whole.

Investigative Research Required for New Technical Development

Although the definition of basic research which is generally applied today is ambiguous, basic research by enterprises can be categorized into three types. One of them is conducted by logical corroboration while analyzing various phenomenons. There is also investigative research from theoretical standpoints and research in pursuit of principles and theories as a science, which is often seen in universities. Problems which we confront can be logically clarified by conducting new investigative research and constructing new technology by the first two types of basic research. Our company has made efforts in this sense, and expects to continue to do so in the future.

Challenging New Ideas

Up to about 10 years ago, the steel industry in Japan often followed the pattern of other industries in importing technology from the West and industrializing it. The major production processes of the present steel industries have also progressed through this process. However, circumstances have changed in the past 10 years. In the midst of the changing world situation Japan is now compelled to yield its own technology and challenge new ideas. Thus, it has been emphasizing basic research which discloses principles and assembles research from basic steps. The outcome is seen even in the advanced nations today. Japan's technology in the basic field can be said to have come on equal terms with Western nations, if not surpassing them.

Measures for Rapidly Advancing New Material Development

We are slightly behind in new material development, as it is not long since the company started to take up this field. Unless basic research which analyzes basic mechanisms and assembles them is conducted, advancement of new materials will fall behind, even more so than steel. Electronics, biotechnology, and new material have seen quick progress. If the principle is not fully understood, effective measures or new methods cannot be directed properly. Consequently, up-to-date progress cannot be followed without recognition of research as a science.

The social roles of new material and steel are different. While new material is functional, steel is structural. In order to construct society, structural material must be strengthened. The issue is how to secure a stable supply of high quality goods at low cost. In our nation, the social capital is still small. Steel must still play an important role in completing the social capital in Japan.

Just Assessment of New Technology and Inventions

Japan's history in respect to S&T is short compared to Western nations. Thus, we have not been able to assess discoveries and inventions made in Japan with confidence. Unless they were once highly evaluated overseas, we were uncertain of their value. It cannot be denied that the climate of the nation was against pioneer or risk undertakings. However, this will change considerably. The growing confidences by researchers will also strengthen this trend.

The government's budget for basic research was greater in projects with definite goals and lesser in straight, accumulative basic research. Even universities and national research institutes appear to be selecting research themes which are socially appealing.

Compared to the United States, the value of research is underestimated in Japan. Researchers are respected to some extent due to their social status. In the United States, individual ideas are sold at an extremely high price. This is why venture businesses are established. Whereas in Japan there is lack of social treatment when considering the price of patents from research results. How to assess information remains an issue for Japan in the future.

Ability of Japanese Researchers

The abilities of Japanese researchers are far beyond what we estimate. The researchers who we send overseas are, frankly speaking, well appraised and we should be more confident. Although the Japanese are said to have few Nobel Prize winners, it is not altogether Japan's fault as it also concerns selection methods and historical reasons. I believe there are actually not a few researchers with high standards in Japan, but many.

Large sums of money have also become necessary in basic research these days, while the effects of investments cannot be readily seen. However, even in our company, the investment of expensive analyzers has not only made direct contributions but has also greatly helped raise the level of research as a whole.

Promoting Frontier Research

Tokyo PUROMETEUSU in Japanese May 86 pp 34-37

[Text] 1. Necessity of Frontier Research

(1) Basic Research Is Required To Break Through Into a New Age

The remarkable progress in S&T has been contributing to the advancement of the social economy. The large inventions and discoveries have frequently played a definite role in changing the world's industries and social structrue. For example: 1) the invention of transistors by Shockley and others has fundamentally revolutionized the conventional electronics industry; 2) the elucidation of the double helix structure of DNA by Watson and Crick has paved the way for today's genetic engineering; and 3) the invention of the laser by Downs is said to be one of this century's leading inventions, as the extent and depth of its application is immeasurable (Table 1). However, such important inventions and discoveries were seen mostly before the 1950s. As the advent of such important discoveries are seen less in recent years, whether future S&T or moreover the industry, can make marked progress is a matter of concern.

Meanwhile, our technical standards which have reached the top in the world, have been mostly acquired by a catchup type research method which yields technology based on scientific information introduced from abroad. In order to contribute to the world for the construction of a wealthy society in the 21st century, as a member of the advanced nations, Japan must break away from the conventional catchup type S&T and also pioneer in the promotion of basic research to discover new scientific information.

(2) Researchers Must Be Gathered From Wideranging Fields To Promote Basic Research

As already mentioned, the expansion of basic research in advanced technologies is becoming exceedingly important in order to yield great inventions and discoveries which may represent the age. Thus, each research organ must promote basic research while making full use of the existing system. Researchers from wideranging fields must also be gathered in promoting research to cope with the current S&T which has become more complex and highly advanced.

Frontier research is the latest basic research which intends to cope with such demands and acquire new scientific information required in the 21st century. It will handle research which extends over multiple fields beyond the conventional research organization and concentrates on deeper pursuits by gathering researchers from wideranging scientific fields.

Table 1. Important Discoveries and Inventions as Source of Current S&T

Item	Period	Inventor and finder	Outline
1. Discovery of nylon	1930s	Karozaus (United States)	Nylon, a synthetic polymer with excellent properties such as tensile strength was discovered. It was the first change from natural fiber to synthetic fiber.
2. Invention of transistors	1940s	Shockley, Bardeen, Brattain (United States) (Nobel Prize of 1956)	Transistor, a new solid element which amplifies electric signals was discovered to support electronics. It was the first semiconductor element which further advanced to IC and LSI.
3. Elucidation of DNA structure	1950s	Watson (United States), Crick (Great Britain) (Nobel prize of 1962)	A spiral structure by two chains was proposed for DNA which controls heredity of organisms. It took the initiative for DNA recombination technology and genetic research.
4. Invention of laser	1950s	Towns (United States) (Nobel Prize of 1964)	Laser, an artificial light with even wavelengths and phases was invented. It became the base of extensive optical technology including optical communications.

2. Frontier Research Scheme

(1) Frontier Research Shall Be Conducted Under an Internationally Open System by Gathering Researchers With Mobility

Frontier research challenges unknown spheres which could not be reached by conventional methods. Thus, while research will naturally be promoted under certain objectives, the general research system which carries out research according to a detailed plan prepared beforehand will not be altogether efficient. In other words, research which was started under a certain objective should be assessed after a certain period to consider how to forward the research. As the research is repeatedly checked and reviewed, the research theme can be reconsidered, resulting in reorganization of the research staff.

A fully flexible system is a requisite in efficiently promoting such research. As the mechanism of frontier research, a flexibly operated research system

which gathers the optimum talent according to research progress will be formed with a full account of the abovementioned point.

As frontier research handles advanced basic research extending over multiple fields, researchers shall be gathered not only within the nation but also from overseas. Thus, about one-third of the researchers are expected to be invited from abroad under an internationally open system (Table 2).

Table 2. Mechanism and Features of International Frontier Research System (Tentative name)

①	Research system joining research abilities of multiple fields	Invitation of researchers from various fields and from industries, universities, government organs, and overseas
②	Internationally open research system	About one-third researchers, including research leaders invited from overseas
③	Long-term research by fluid exchange of researchers	Continued research as a group while researchers change by terms
④	Active application of young researchers	Usage of young researchers as much as possible except for leaders
⑤	Exploitation of new information endorsed by experiments	Application of latest research facilities
⑥	Establishment of a spot to yield original ideas in a free and open atmosphere	Opening of a standing forum for researchers of different specializing fields and different scientific fields from the nation and abroad to exchange opinions

(2) A Comprehensive Supportive System Is Required for Promotion of Frontier Research

Backing up a mobile system is especially required in the promotion of frontier research which demands high-degree mobility. In other words, a supportive system which enables the following items is a requisite.

1) Steady accumulation of research outcome and smooth operation of research even after researchers are changed.

2) Smooth adjustment, maintenance, etc., of research facilities and equipment.

Such a research system differs from the conventional research system. A conventional research structure and a different operation formation will be established at an existing research organ which supports a mobile research group in the promotion of frontier research.

As the Institute of Physical and Chemical Research is the only general research organ in our nation which has the proper researchers and facilities required in research fields based on S&T such as physics, chemistry, engineering, and life science, it is the optimum research center to conduct frontier research. Moreover, the institute has exchanged tieups with many other research organs (Maxplank Research Institute of West Germany, Pasteur Research Institute of France, the Commonwealth Science Laboratory Research Organization (CSLRO), etc.,) in the past, which was a great advantage in securing capable researchers.

Accordingly, frontier research shall be conducted at the Institute of Physical and Chemical Research based on the International Frontier Research System (tentative name) which will be set up to distinguish its operation from conventional research and apply the special features of frontier research.

(3) Frontier Forum Will Be Permanently Set Up on the Spot To Produce Original Ideas in a Free Atmosphere

It is important for researchers of different fields to stimulate each other in order to secure the originality required in basic research. Thus, a kind of salon where many researchers can stop by and exchange information will be established in the International Frontier Research System (tentative name). Moreover, a general forum beyond research fields will be held twice a year and a separate forum for the respective research fields is expected to be held as occasion demands (Figure 1).

3. Frontier Research Starting From 1986

(1) Research Concerning 1) Homoestasis of Organisms and 2) Frontier Material Will Be Promoted From FY 1986

In order to discover new scientific information which may become the base of the 21st century's technological innovation, prospective fields which extend over multiple fields and have high potentialities of containing important new information must be selected for frontier research.

Research fields started in FY 1986 concerning: 1) substance and material related S&T; 2) information and electronic related S&T; and 3) life science which may become the base of future S&T were selected among the themes raised in report No 11 "Prospective Basic and Initiative S&T" of the Scientific and Technical Council, as follows:

--Organisms--research on homoestasis of living bodies--life science
--Substances--research on functional substances (frontier material)--substance and material, information and electronics related technology

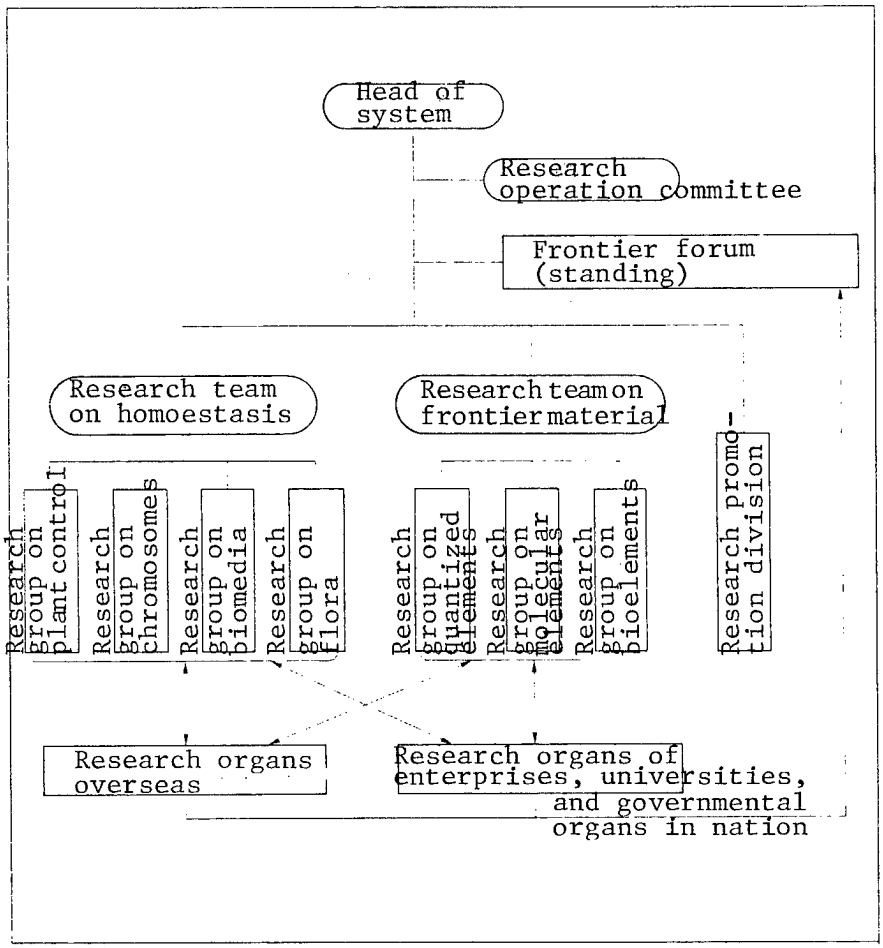


Figure 1. International Frontier Research System (tentative name)
(Inner organ of Institute of Physical and Chemical Research)

These subjects were also suggested as prospective research fields to rapidly advance by the U.S. National Academy of Science (NAS) in 1983, in reply to the U.S. Congress. Because these fields are attracting the attention of many researchers, they may be considered appropriate for frontier research.

These are long-term projects which will require 15 years, or 3 terms, as 1 term lasts 5 years.

(2) Outline of Research

1) Research fields of homoestasis of living bodies

--Elucidation of homoestasis of animals and plants

--Expected application fields: elucidation of the causes of aging which is still mostly unknown today, controlling aging, creation of resistant plants, etc.

Various phenomenon which generate from combining cells, biomolecules such as protein, polymers, substances such as metal and their infinitesimal conditions will be elucidated, with the expectation to yield frontier materials (new functional elements, etc.) which may become the basis of new fields such as information science.

(3) Outline of FY 1986 Budget

The abovementioned frontier research will be started from October 1986 with ¥1,120 million budget which is presently appropriated in the FY 1986 Budget Bill.

(Items of Budget Bill)

①	Research expenses	¥ 500 million
②	Expenses to invite researchers, etc.	¥ 190 million
③	Facility expenses (construction of research center, laboratories, accommodations for foreigners)	¥1,010 million (in bond)
		¥ 430 million

System for Promoting Original S&T

Tokyo PUROMETEUSU in Japanese May 86 pp 42-43

[Text] Exploratory Research for the Advanced Technology System was established in October 1981 with the Research Development Corp. of Japan as its main operational body, in order to take a lead in basic research which was recently regarded with high priority. It has entered into its fifth year. In less than 5 years, the international position of our nation in the R&D field has become even more important and strict. This system has drawn the attention of various nations as an initiating and unique system and has also produced many original results, one after another.

1. Features of the System

It has been repeatedly said that our nation lacks originality and creativity in R&D. In order to promote original R&D, factors considered to have obstructed originality in R&D in the past have been removed as much as possible and various bold and new ideas have been adopted in this system as follows:

(1) Investigative research without a detailed research target or application goals will be conducted by setting a research field which has a high potentiality of creating innovative technology.

(2) Young and capable researchers will be gathered from industries, universities, governmental organs, as well as from overseas to conduct research for a definite period (5 years) under a general director who has advanced knowledge and leadership.

(3) The general director will be authorized to change the research plan according to the progress of the research and his judgment, whenever necessary, in order to forward flexible operation.

(4) The Research Development Corp. of Japan will not retain its own research facility. Instead, existing research centers, etc., of enterprises will be rented.

(5) As an incentive to urge capable researchers to join research projects, research patents will be owned jointly by the Research Development Corp. of Japan and individual inventors. The holdings of researchers who belong to a certain organ may be placed under the authority of this organ.

2. Present Conditions of the System

The system which started off with four research projects, namely, "Superfine Particles," "Special Structural Matters," "Fine Polymer," and "Perfect Crystal" in FY 1981 has continued to supplement other research projects every year. Nine research projects are located at 26 areas from Sendai at the far north to Tokushima at the far south.

Owing to the outcome of numerous research, there were 276 patent applications and 506 reports or theses presented in academic meetings as of 1 February 1986.

3. Outline of FY 1986 Budget Bill

In FY 1986, four research projects which started in 1981 will terminate their research terms of 5 years at the end of September. Meanwhile, three projects namely, "Flux Quantum Information," "Supermolecule," and "Biohoton" will start in place of these previous projects. A budget of ¥2,687 million (estimate of ¥2,570 million in FY 1980) is appropriated in the FY 1986 Budget Bill.

The outline of the newly starting research projects in FY 1986 are as follows:

(1) Flux Quantum Information

As electric current flows through a metal ring, a magnetic flux passing the metal ring is formed. The magnetic flux is known to take double the integer (flux quantization) with an infinitesimal unit under superconductive conditions.

Meanwhile, the recent advancement of low temperature S&T and fine processing technology is about to realize artificial control of flux quantum of infinitesimal units.

With an eye on the extremely high speed and low energy consuming movements compared to semiconductor elements, the generation of flux quantum and electric and magnetic phenomenon which occur while it is transmitted will be elucidated. Methods to control the flux quantum and the possibility of its application in information processing and ultraprecision measurement, etc. will be pursued.

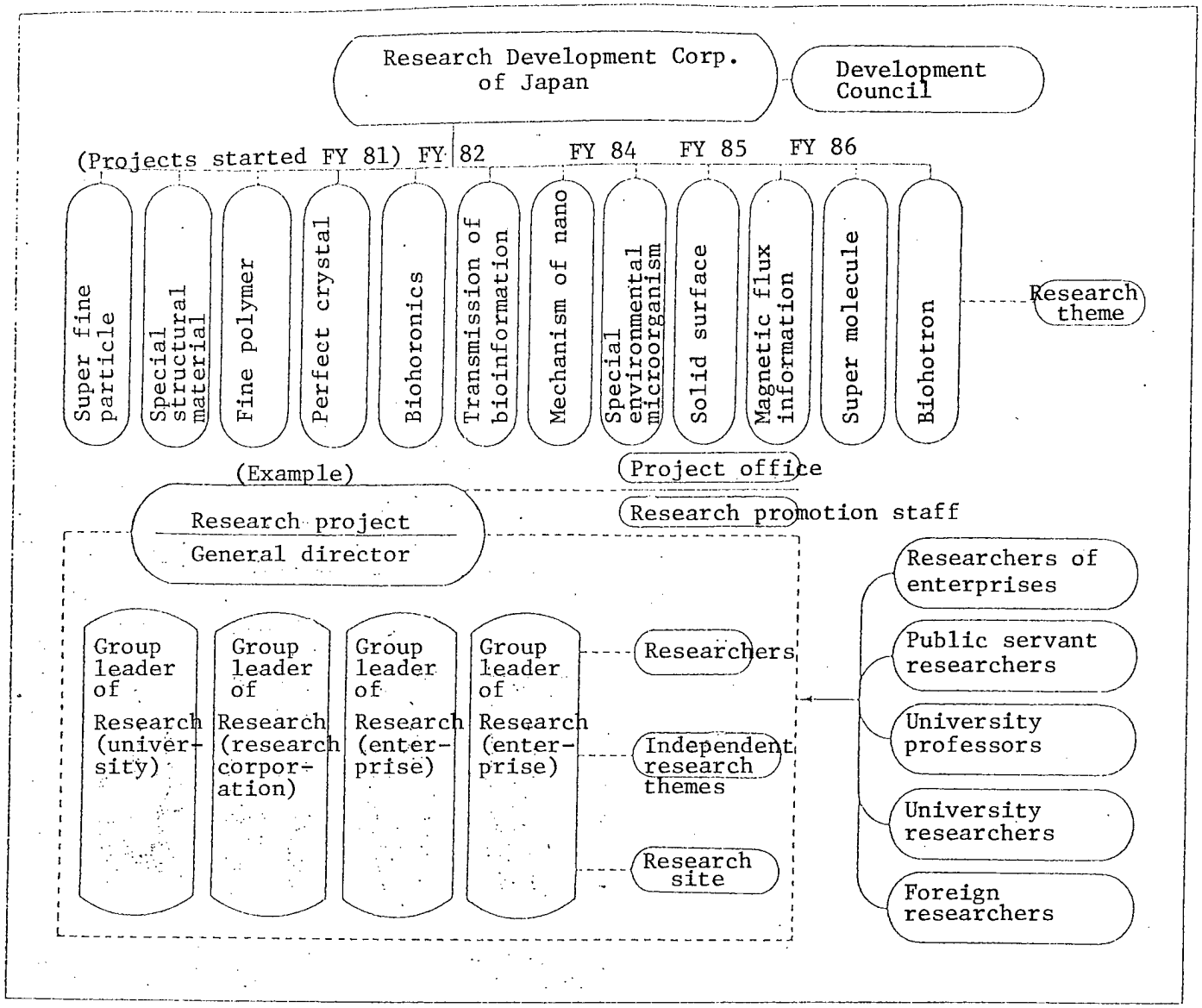


Figure 1. System Mechanism

(2) Superfine Particle

The aggregate body (superfine particle) of polymers of protein, lipids, etc., which composes living bodies possesses high-level organic functions such as energy conversion by muscle proteins or information transmission by genes. These functions are generated by a mechanism (loose coupling mechanism) which operates by making use of environmental changes. Compared to the clockwork mechanism which outputs according to inputted information regardless of environmental changes as with precision equipment such as measuring devices, the fundamental factor which makes organisms function as an organism is seen in this loose coupling mechanism.

With an eye on the loose coupling mechanism, the construction which generates this mechanism in organisms will be elucidated and possible applications in engineering fields such as making new mechanical contrivances will be pursued under this research theme.

(3) Biohoton

Biohoton consists of light which is mutually related to organisms and related substances (enzymes, lipids, protein, etc.,). Much research has been conducted in the past on the interaction between organisms and light from the standpoint of "photosynthesis" as an energy. This function is recently spotlighted for playing an important role in supplying information to the inner part of organisms. Reversely, controlling bioreaction by using light is also considered.

With an eye on the close relationship between organisms and light which leads to a new research in biotic phenomenon, the characteristics of ultra-faint light which is emitted from living cells will be elucidated and its luminous origin will be pursued, in order to search a method which seeks the conditions inside the living bodies by emitted light. Metabolismwhich occurs in the cell or activation of cells when faint laser beams, etc., are radiated on organisms will also be elucidated in this research. Application of this research in pathologic diagnosis or treatment, growing agricultural products, and in quality control will also be investigated.

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